CFRA

Industry Surveys

Pharmaceuticals

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Wan Nurhayati, CFA
Equity Analyst

Siti Salbiah
Industry Analyst

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Contacts

Sales Inquires & Client Support
800.220.0502
cservices@cfraresearch.com

Media Inquiries
press@cfraresearch.com

CFRA
977 Seminole Trail, PMB 230
Charlottesville, VA 22901

Contributors

Stewart Glickman, CFA
Equity Analyst

Raymond Jarvis
Senior Editor

Atifi Kuddus, Geraldine Tan
Associate Editors

Marc Bastow
Contributing Editor

CHARTS & FIGURES

NEW THEMES

What's Changed: The total global spending on cell, gene, and RNA-based therapies is expected to reach $20 billion by 2026, albeit with uncertain clinical and commercial successes. Read more on page 24.

What's Changed: Share prices of several pharmaceutical companies, such as Sanofi and GSK, have recently been impacted by litigation risk. Check out page 26 for more information.

What's Changed: We added a new table listing the top 10 largest legal settlements made by pharmaceutical companies on page 27.

EXECUTIVE SUMMARY

Our outlook for the Pharmaceuticals industry for the next 12 months is neutral.

Key Products and New Launches are Back as Main Growth Drivers

With the anticipated dwindling Covid-19 related sales going forward, we expect growth over the next 12 months to be supported by key products and new launches. According to Evaluate, among the biggest projected product launches in 2022 (with potential blockbuster status by 2026) are Eli Lilly's Donanemab (for Alzheimer's disease), Roche's Gantenerumab (for Alzheimer's disease), Bristol Myers Squibb's Deucravacitinib (for psoriasis and other autoimmune diseases) and Mavacamten (for cardiomyopathy), and Amgen/AstraZeneca's Tezepelumab (for severe asthma). Topline growth, however, is expected to decelerate in 2022 and 2023 (vs 2021), partly due to the expectation of lower Covid-19 related sales and tough comparison base.

Less Contribution from Covid-19 Related Sales Going Forward

We expect to see less contribution from Covid-19 related sales going forward amid improving health situation, particularly compared to the peak in 2021. We note majority of the companies that previously benefited from the surge in Covid-19 related products during the height of the pandemic (vaccine, diagnostic/testing) are now guiding for lower or more stable Covid-19 related sales in 2022. We expect booster shots (amid concerns of the waning protection against Covid-19 infection and hospitalization over time, as well as the concern of the threat of new variants) and Covid-19 drugs and treatment to support Covid-19 related sales going forward, although not as significant as the primary vaccines.

Continuous Pricing Pressure

We expect the Pharmaceuticals industry to continue facing pricing pressure going forward. The participation in the National Reimbursement Drug List (where pharmaceutical companies agreed to cut drug prices in order to gain access to the list that allows them to enter the Chinese market) and the Volume-Based Procurement Program in China is putting pressure on margin, although we acknowledge the importance of this market given its sheer size and potential volume growth. Another source of pricing pressure could come from the U.S. Inflation Reduction Act 2022, although this will only be effective from 2026. High drug prices in the U.S. remain a big political issue where both the Democratic and Republican parties aim for more affordable drug prices for Americans. Among others, the Act allows the U.S. Department of Health and Human Services (HHS) to negotiate prices for certain high-cost Medicare covered drugs, starting initially with 10 drugs in 2026 (and ramping over time to a total of ~100 drugs by 2031). HHS will select and publish the list of selected drugs subject to price negotiation at least two years prior to the initial price applicability year. The negotiation-eligible drugs will be selected from a list of Part D and Part B with the highest total expenditures. While it is not clear which drugs would be negotiated, we see those at the top end of the most expensive drug list to be at risk.

PHARMACEUTICALS

Outlook: Neutral

MARKET CAP BREAKDOWN*

RANK NO.	COMPANY NAME	MARKET CAP ($ billion)
1	Johnson & Johnson	454.8
2	Eli Lilly	344.0
3	Roche	274.0
4	Pfizer	261.3
5	Novo Nordisk	246.0
	Others†	1,656.1

Source: CFRA, S&P Global Market Intelligence.
**Data as of October 31, 2022.*
†Refer to the "Comparative Company Analysis" section of this survey for the list of companies.

ETF FOCUS

XLV Health Care Select Sector SPDR Fund	AUM ($M) 37,072.0	Expense Ratio 0.10
VHT Vanguard Health Care	AUM ($M) 15,601.8	Expense Ratio 0.10
IHE iShares US Pharmaceuticals	AUM ($M) 388.0	Expense Ratio 0.39
XPH SPDR S&P Pharmaceuticals	AUM ($M) 211.9	Expense Ratio 0.35

BY THE NUMBERS

5.4% 2021-2026 CAGR global prescription drug sales

4.2% 2021-2026 CAGR for global R&D spending

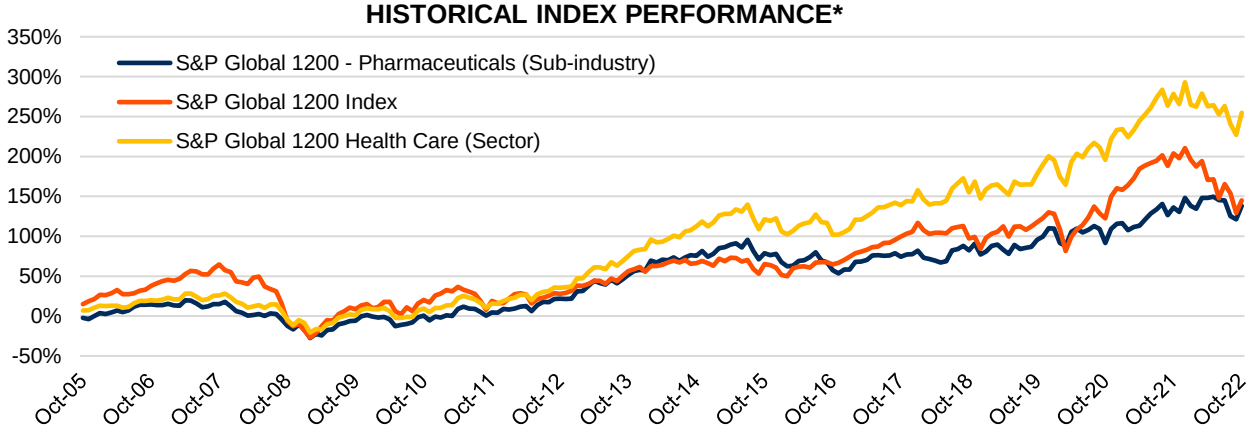
$196 billion New brand spending in developed markets over 2022-2026

$188 billion Impact of exclusivity losses in developed markets over 2022-2026

9-12% 2022-2026 CAGR for global oncology spending

10 Drugs in negotiation list under the U.S. Inflation Reduction Act in 2026

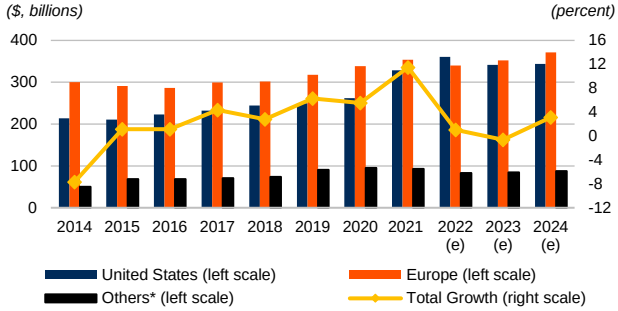
HISTORICAL INDEX PERFORMANCE*



*Data through October 31, 2022.
Source: S&P Global Market Intelligence.

FINANCIAL METRICS

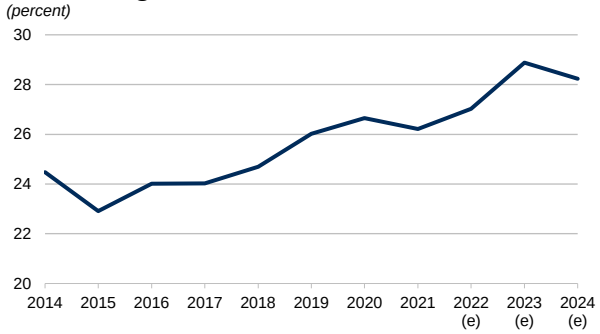
Revenue Growth



*Refer to the Comparative Company Analysis section for other companies.
e-Estimated.
Source: CFRA, S&P Global Market Intelligence.

- Industry revenue grew by 11.5% in 2021, lifted by the contribution from Covid-19 vaccine sales for vaccine makers like Pfizer.
- We expect industry revenue growth to decelerate to 1% in 2022 and -0.6% in 2023, partly due to the expectation of lower Covid-19 related sales amid improving health situation, as well as tough comparison base.

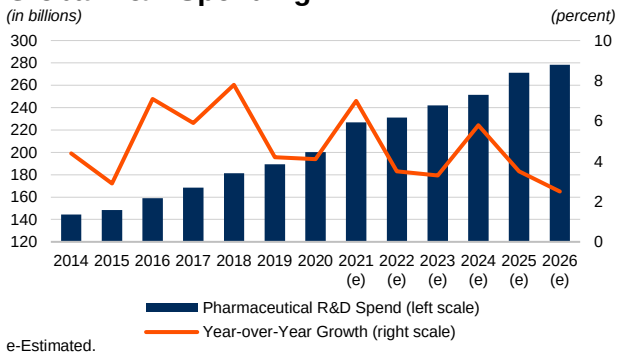
EBIT Margin



e-Estimated.
Source: CFRA, S&P Global Market Intelligence.

- EBIT margins improved from 2015 to 2021, largely supported by the implementation of cost-saving initiatives.
- We expect the ongoing cost-saving measures to cushion the continued pricing pressure going forward.

Global R&D Spending

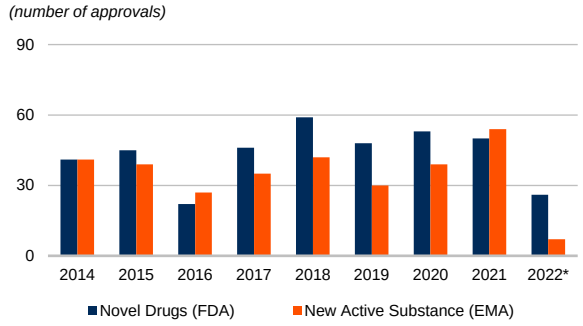


e-Estimated.
Source: Evaluate.

- Research & development (R&D) spending is expected to increase due to pharmaceutical companies' continuous efforts to boost their drug pipelines amid upcoming patent expirations, at a CAGR of 4.2% between 2021 and 2026, according to Evaluate.
- This is a slightly slower growth than historical CAGR of 4.7% between 2012 and 2020, which could be attributed to the continuous effort in improving R&D processes (*e.g.,* by using big data analytics or artificial intelligence), in our view.

KEY INDUSTRY DRIVERS

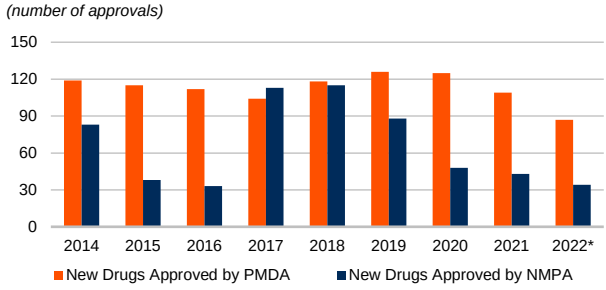
Drug Approvals by FDA & EMA



*FDA Approvals as of September 2022. EMA Approvals as of October 2022.
Source: U.S. Food and Drug Administration, Europe Medicines Agency.

- The U.S. Food and Drug Administration (FDA) approved 26 novel drugs year-to-date as of September 30, 2022, and 50 novel drugs in 2021, which is at a near similar level to the past five-year average.
- The European Medicines Agency (EMA) recommended 10 medicines for approval at its October 2022 meeting, of which 7 contain a new active substance and 3 generic medicines.

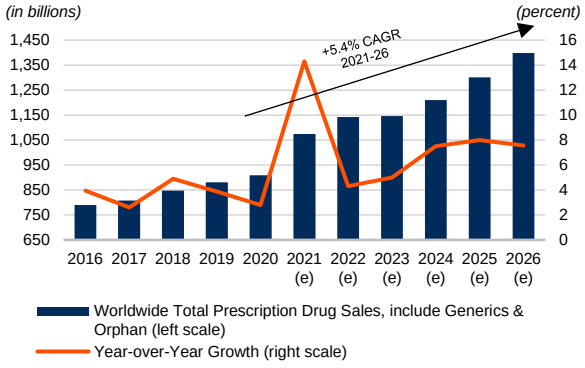
Drug Approvals by PMDA & NMPA



*Data as of August 2022.
Source: National Medical Products Administration (NMPA), Pharmaceuticals and Medical Devices Agency (PMDA).

- Over the past few years, Japan's Pharmaceuticals and Medical Devices Agency (PMDA) has accelerated drug development and new drug approval to allow for faster access to medicines for patients. As of August 2022, PMDA recommended 87 new drugs for marketing authorization for the year.
- Year-to-date as of August 2022, China's National Medical Products Administration (NMPA) granted marketing approvals to 34 new drugs.

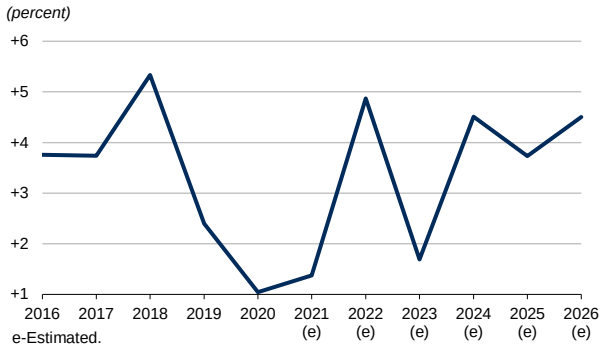
Worldwide Total Prescription Drug Sales



e-Estimated.
Source: Evaluate.

- Worldwide prescription drug sales are forecast to grow at a 5.4% CAGR from 2021 to 2026, hitting $1.4 trillion in 2026. Evaluate expects Merck & Co to overtake Pfizer as the leading prescription drug company in 2026, with sales of $63.7 billion.
- We think the growing aging population, lengthening of life expectancy, and rising chronic disease prevalence will drive long-term demand for better quality drugs in the years ahead.

Global Drug Sales at Risk from Patent Expiration



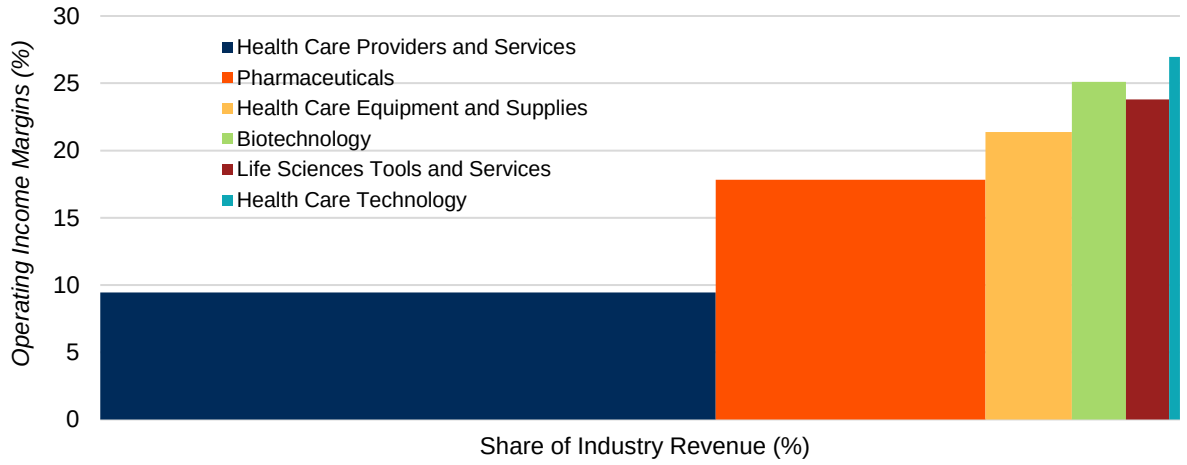
e-Estimated.
Source: Evaluate.

- Novel drug makers receive multi-year periods of exclusivity to market their drugs once the formulations are patented and approved by regulators. Down the road, however, loss of exclusivity from patent expirations or successful patent challenges from competitors can cause major sales declines for brand drugs.
- Evaluate expects $226 billion of sales to be at risk between 2021 and 2026, with 2023 set to see the expiry of key patents for several biologics, including Stelara.
- In 2025, Bristol Myers' Pomalyst, Pfizer's Xeljanz, and Boehringer Ingelheim's Ofev are set to lose exclusivity.

INDUSTRY TRENDS

PROFIT POOLS

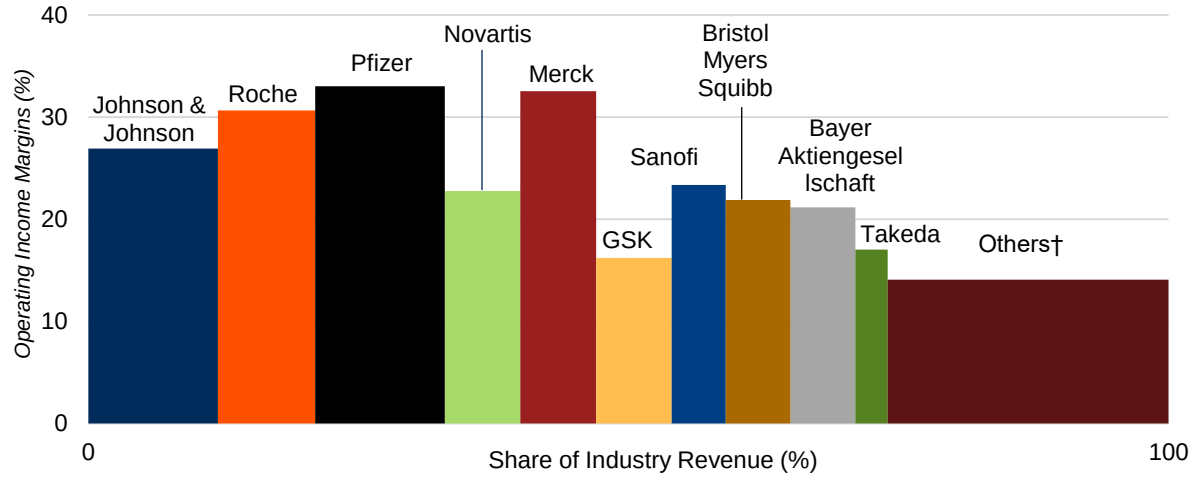
PROFIT SHARE MAP OF THE GLOBAL HEALTH CARE SECTOR
(last twelve months through second quarter of 2022)



*Companies within the S&P Global 1200 Index as of September 30, 2022.
Source: CFRA, Company Reports.

The Pharmaceuticals industry is the second-largest industry (in terms of total revenue) in the global Health Care sector and boasted the fifth-highest EBITDA margins as of the second quarter of 2022. Pfizer is the biggest individual revenue contributor to the industry, representing 12.8% of industry revenue and has the highest operating margin (33%) during the same period, among the largest pharmaceutical companies globally. (Our profit pool analysis is based on constituents of the S&P Global 1200 index.)

PROFIT SHARE MAP OF THE GLOBAL PHARMACEUTICALS INDUSTRY
(last twelve months through second quarter of 2022)

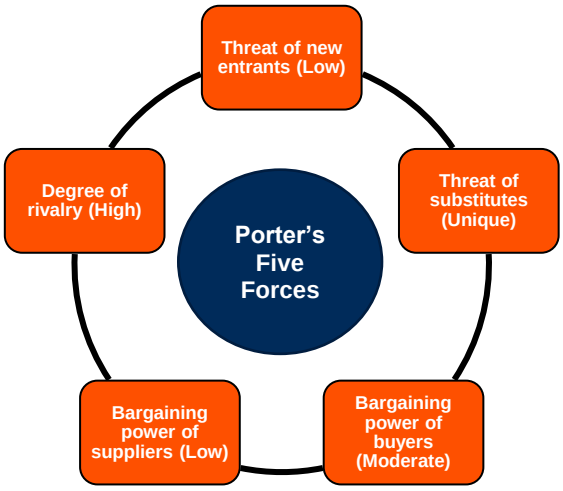


*Companies within the S&P Global 1200 Index as of September 30, 2022.
†Refer to Comparative Company Analysis section of this survey for other companies in the industry.
Source: CFRA, Company Reports.

Competitive Environment

PORTER'S FIVE FORCES

Porter's five forces, which provide a framework for industry analysis, were formulated by Michael E. Porter of Harvard Business School in 1979. Here are the five parameters on which an industry can be analyzed, and how these apply to the Pharmaceuticals industry.



PHARMACEUTICALS INDUSTRY: PORTER'S COMPETITIVE MATRIX

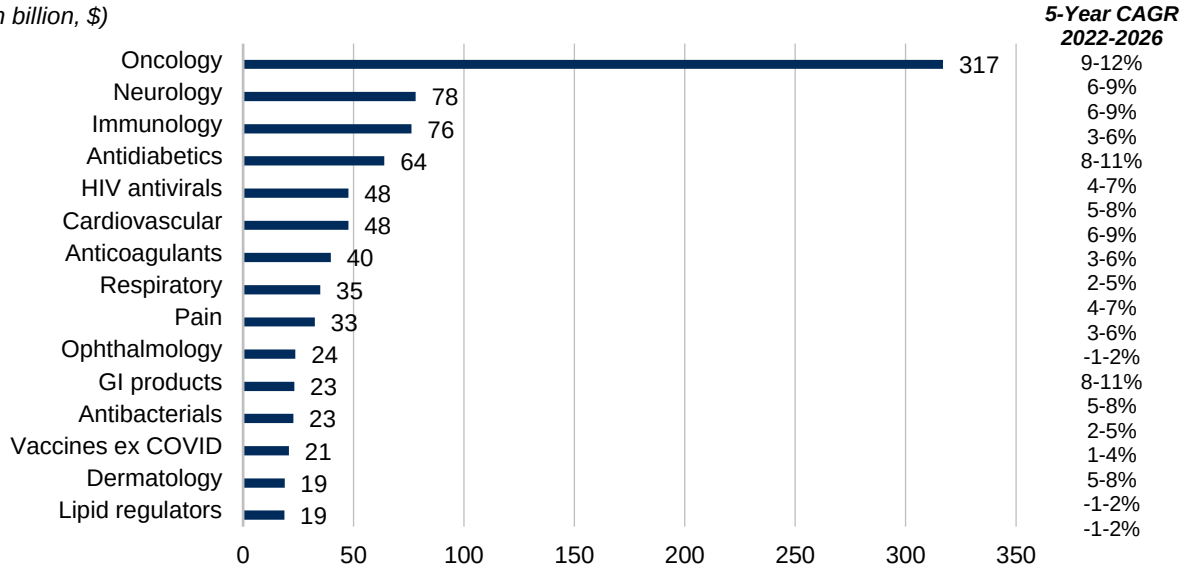
Threat of New Entrants (Low)	The Pharmaceuticals industry has a high barrier to entry mainly due to the significant investments needed for a company to properly establish the R&D, manufacturing, marketing, and distribution units. Given the nature of the business, there is a risk of zero returns if the company fails to produce the required drugs in time, resulting in large losses for investors. Regulatory constraints such as lengthy approval time and process also deter new entrants to the industry.
Threat of Substitutes (Unique)	A new regulator-approved drug that has patent protection has essentially no substitutes. However, once a drug loses its patent and/or exclusivity rights, generic production begins, and the number of substitutes increases rapidly due to the cheaper prices from the absence of high costs associated with R&D.
Bargaining Power of Buyers (Moderate)	Pharmaceutical companies are able to control brand drug prices during the patent protection period (typically 10 to 20 years) but will face intense pricing competition after generic competition enters the market. The rise in the number of producers of a given drug significantly increases customers' bargaining power. Also, large customers such as hospital networks or pharmacy benefit managers negotiating on behalf of large health insurers generally command much greater bargaining power compared with individual customers who have little to no bargaining power.
Bargaining Power of Suppliers (Low)	Drug manufacturers generally require raw materials, manufacturing equipment, and packaging materials from external suppliers, while the remaining expenses are focused on internally managed R&D efforts. Given that the production inputs are readily obtainable from numerous sources, suppliers have limited power to bargain or influence prices.
Degree of Rivalry (High)	The low switching cost and low product differentiation mean significant rivalry within the industry. There are also many participants in the Pharmaceuticals industry ranging from small to large firms whose brand drugs often compete with each other on similar treatment indications, as well as against generic challengers who seek to shorten patent protection periods. The increase in patent expiration has spurred the growth in generics, thus further fueling competition.

Source: CFRA.

Oncology Remains the Largest Therapy and Projected to Grow the Fastest Through 2026
Pharmaceutical companies compete across a diverse range of therapeutic areas. An important aspect of corporate strategy for a drug company is determining which areas to focus its drug development efforts on. Oncology is the largest therapy area in terms of global prescription drug sales with a 15.9% share in 2021. Notably, four key oncology drugs manufactured by Merck & Co (Keytruda), Bristol Myers Squibb (Opdivo), Roche (Tecentriq), and AstraZeneca (Imfinzi) made up 17.4% of worldwide oncology sales in 2021. While the development of vaccines gained traction since 2020 due to the Covid-19 pandemic, oncology is still expected to remain the largest therapy area going forward, where Evaluate forecasts it to account for 22% of prescription drug sales in 2026. According to Evaluate, the growth is expected to be driven by the booming immune-oncology sub-category, led by products such as Keytruda and Opdivo. The combined annual sales of the two drugs are expected to grow to $43.5 billion in 2026 from $24.4 billion in 2021. According to IQVIA, oncology is projected to add 100 new treatments over 2022-2026, which includes innovative treatment through cell therapy, RNA therapy, and immuno-oncology treatments, contributing nearly $120 billion in new spending and bringing the total market to more than $300 billion in 2026. CFRA thinks the oncology market will continue to see significant growth due to the rising number of cancer patients worldwide. According to estimates from the American Cancer Society, in 2020 (latest available), there were 19.3 million new cancer cases and almost 10 million cancer deaths worldwide. By 2040, the global burden is expected to grow to 28.4 million new cancer cases and 16.3 million cancer deaths simply due to the growth and aging of the population.

While many therapy areas are expected to grow slower than historical partly due to the impact of biosimilars, neurology is one of the few exceptions with new therapies including greater use of novel migraine therapies, potential treatments for rare diseases, and the potential for therapies for Alzheimer's and Parkinson's expecting to contribute to the rapid acceleration of the neurology market.

2026 GLOBAL SPENDING OF TOP 20 THERAPY AREAS
(in billion, $)



Source: IQVIA.

TOP 10 SELLING PRODUCTS WORLDWIDE BY 2026

(ranked in terms of 2026 product sales, in billions of U.S. dollars)

RANK	PRODUCT	COMPANY	THERAPY AREA	COUNTRY	MARKET STATUS	WORLDWIDE PRODUCT SALES ($ billion)		2021-2026 CAGR (%)
						2022*	2026	
1	Keytruda	Merck & Co	Oncology	Switzerland	Marketed	10.1	29.8	19.9
2	Eliquis	BMS	Blood	U.S.	Marketed	6.4	13.8	13.5
3	Dupixent	Sanofi	Immunomodulators	U.K.	Marketed	3.6	13.2	24.4
4	Ozempic	Novo Nordisk	Endocrine	U.S.	Marketed	5.4	13.1	16.0
5	Darzalex	J&J	Oncology	U.S.	Marketed	3.8	12.6	21.9
6	Opdivo	BMS	Oncology	U.S.	Marketed	4.0	12.6	21.1
7	Biktarvy	Gilead Sciences	Systemic Anti-infectives	Switzerland	Marketed	4.7	11.6	16.3
8	Comirnaty	Pfizer	Systemic Anti-infectives	U.S.	Marketed	3.6	10.7	19.8
9	Trikafta	Vertex	Respiratory	U.S.	Marketed	3.7	10.0	18.2
10	Skyrizi	AbbVie	Dermatology	U.S.	Marketed	2.2	9.3	27.3
					Total	**47.4**	**136.7**	**19.3**

*As of Q2 2022.

Note: Sales represent company reported sales where available, otherwise based on an average of equity analyst estimates.

Source: Evaluate.

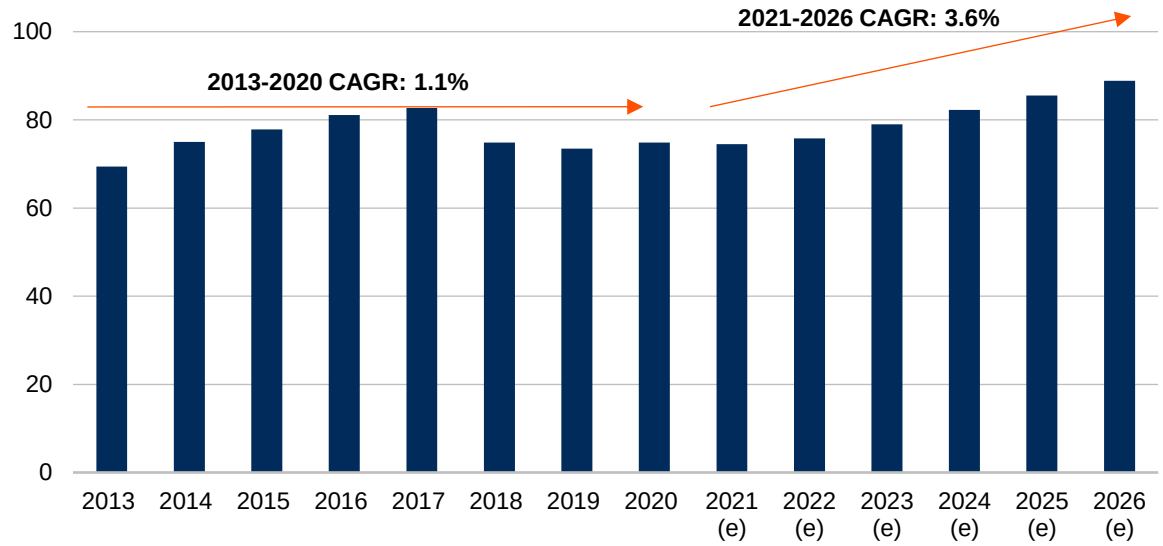
The Continuous Threat of Generics and Biosimilars

As drugs continue to come off patent, the market is turning toward generic substitution. Generic medicines play an important role in health care across the world, accounting for the majority of total medication dispensed while contributing only a fraction of the cost. In 2021, global spending on unbranded generic medicines reached $153.8 billion, according to IQVIA.

Key players in the generic drugs market include Viatris, Teva Pharmaceuticals, Sun Pharmaceutical, and Sandoz (Novartis generic arm). In terms of country, India is the largest provider of generic drugs globally, exporting to major markets, including the U.S. (which accounts for roughly 40% of U.S. generic drugs import) and the European Union (EU). CFRA thinks India-based generic makers will continue to take market share from developed nation firms due to lower production costs. On the other hand, we note the primary focus of many companies in China is moving toward innovative drugs, and we expect Chinese pharmaceuticals companies to shift some of their resources away from generics and focus on the more lucrative innovative drugs.

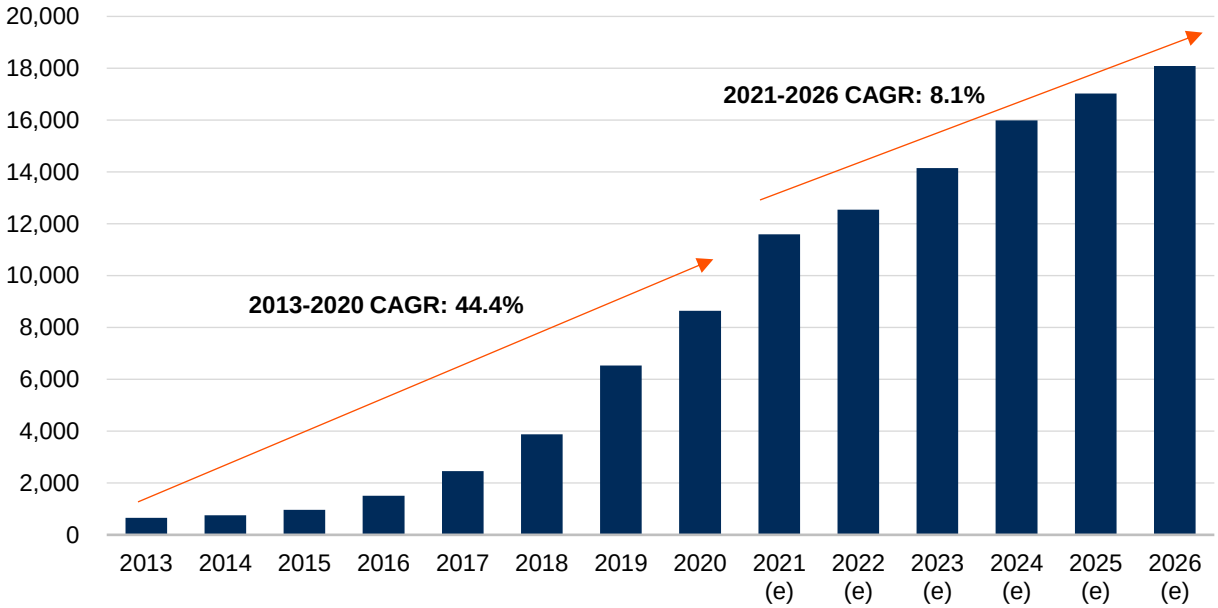
According to Evaluate, worldwide generics sales are expected to grow by 3.6% CAGR over the 2021 to 2026 period to $89 billion and make up about 7%-8% of total prescription drug sales.

WORLDWIDE TOTAL GENERIC DRUGS SALES (2013-2026)
(in $, billions)



Source: Evaluate.

WORLDWIDE BIOSIMILARS MARKET OUTLOOK
(in $, billions)



Source: Evaluate.

Aside from generics, the biosimilars market is also growing rapidly and accounts for a substantial and increasing portion of health care costs. A biosimilar is a biologically equivalent form of a biologic drug, somewhat analogous to a generic form of a branded drug, although there are differences both in composition and approval processes for biosimilars versus generics. Biologics and biosimilars generally consist of complex organic (sometimes living) compounds, which are often grown in living systems rather than synthetically manufactured as traditional drugs are. After facing challenges in its early years, the biosimilars market grew significantly over the year, helped by the streamlining of regulatory guidelines as well as increasingly positive clinical data, which led to better perception (of biosimilars) by various health care stakeholders.

The EU pioneered the regulation of biosimilars since the first approval of the growth hormone Somatropin in 2006, while the U.S. FDA gave the first approval for biosimilar in 2015. Since then, the number of biosimilar approvals and, subsequently, biosimilar sales have gradually increased. Evaluate expects biosimilar sales to grow by 8.1% CAGR over the 2021 to 2026 period. In our view, the higher projected growth for biosimilars compared to generics can be partly explained by the upcoming loss of exclusivity of several key biologics such as Stelara and Humira.

Biosimilars are typically priced at about a 30% discount, while generic drugs are typically priced at an 80%-85% discount to the originator's compound.

OVERVIEW OF THE MAJOR PHARMACEUTICAL MARKETS

MAJOR PHARMACEUTICAL MARKET	PHARMACEUTICAL SALES (in $, billions)		R&D SPENDING* (in $, billions)	HEALTH CARE SPENDING AS A PERCENTAGE OF GDP (%)		2022-2026 CAGR GLOBAL INVOICE MEDICINES SPENDING (%)
	2020	2021	2020	2020	2021	
U.S.	533.5	550.0	72.4	18.0	17.8	2.5-5.5%
Europe						
Germany	56.6	-	7.6	12.5	12.8	4.5-7.5%
France	37.8	-	4.3	12.4	12.2	2-5%
Italy	33.4	-	1.6	9.7	9.5	2-5%
U.K.	28.7	-	5.5	12.8	11.9	4-7%
Spain	26.3	21.2	1.1	10.7	-	1.5-4.5%
Switzerland	7.3	7.1	7.2	11.8	-	-
China	93.0	98.5	10.9	-	-	-
Japan	79.2	72.0	88.9	11.1	-	-2-1%

*R&D spending latest available data as of 2020.

Source: IQVIA, OECD, EFPIA, CSET, JPMA.

United States

The U.S. is the world's largest pharmaceutical market, generating over $550 billion in sales in 2021. Many of the leading global pharmaceutical companies are based in the U.S., including Pfizer, Merck & Co, and Johnson & Johnson. The primary reason most pharmaceutical firms focus heavily on the U.S. market is because they can generally charge more for brand drugs in the country. This is mainly because health care customers in the U.S. are private and fragmented, and drug makers do not have to negotiate pricing with a centralized national health system. However, the Inflation Reduction Act of 2022 is expected to lower drug prices in the U.S. Among others, the Act allows the government to negotiate prices on the costliest prescription drugs, although this will only be effective from 2026.

Europe

◆ Germany

Germany is Europe's largest pharmaceutical market, ranking first in terms of pharmaceutical sales and R&D spending as of 2020 (latest available). Biologics have taken up a considerable share of the pharmaceutical market in Germany, according to Germany Invest & Trade, growing by 11.6% on average annually from 2015 to 2019 (latest available), more than twice the growth of the overall pharmaceutical market. The total revenue of biopharmaceuticals in Germany accounted for more than a quarter of the market for pharmaceuticals.

◆ **France**

France came in second in Europe in terms of sales as of 2020 (latest available) and ranked fifth largest worldwide. France's health care spending in relation to its GDP reached 12.2% in 2021 from 12.4% in 2020, according to the Organisation for Economic Co-operation and Development (OECD). Although France has strong capabilities in the life sciences area, the country is relatively weak in terms of the number of biotech firms, with only 913 as of October 17, 2022, behind the U.K. and Germany.

◆ **Italy**

Italy is Europe's third-largest pharmaceutical market in 2020 (latest available). The country has several major players consisting of small and medium-sized companies, as well as large private family-owned firms. Unlike other European countries such as Germany (Bayer and Merck KGaA) and France (Sanofi), Italy does not play host to any giant pharmaceutical companies. Since 2004, the Italian government has implemented an aggressive program to hold down pharmaceutical costs. Italy has a lower pharmaceutical spending compared to other major European countries, with health care spending accounting for 9.5% of GDP in 2021, about 0.2 percentage points below the OECD average of 9.7% in 2020, according to the OECD.

◆ **United Kingdom**

The U.K.'s pharmaceutical market was the fourth-largest market in Europe and ranked third in Europe in terms of R&D spending in 2020 (latest available), behind Switzerland. It is the home of large pharmaceutical companies AstraZeneca and GSK. The U.K. spent 11.9% of its GDP on health care in 2021, above the OECD average of 9.7% in 2020.

◆ **Spain**

Spain ranked fifth in Europe in total pharmaceutical sales in 2020 (latest available) but lags in pharmaceutical innovation, with total R&D spending ranking in the No. 6 spot in Europe in the same period. Following the 2009 economic crisis, health care spending remained flat or even decreased in some years but started to rise again from 2014 onward. In 2015, Spain implemented a pharmaceutical budget cap in order to contain expenditure and link it to GDP growth. Spain's health care spending as a percentage of GDP in 2020 (latest available) of 10.7% was higher than the OECD average of 9.7% in the same year.

◆ **Switzerland**

The Pharmaceuticals industry is one of Switzerland's most important growth drivers and export sectors. The industry has been responsible for more than a third of the country's GDP growth over the last decade. Switzerland also has a large export surplus of pharmaceutical products worldwide, with pharmaceutical exports making up more than 40% of Swiss exports. The country ranked second in Europe in terms of R&D spending in 2020 (latest available) and is the home to pharmaceutical giants Roche and Novartis. Many international pharma and biotech companies have also invested in Switzerland, as the country offers flexible labor laws and a stable economic environment. One of the world's leading biotech hubs, Switzerland provides nearly 50,000 jobs in the Pharmaceuticals industry, and more than 1,000 biotech start-ups work in fields ranging from dermatology to oncology, from neurology to antibodies.

Asia-Pacific

◆ **China**

China's Pharmaceuticals industry has been growing rapidly over the years, driven by central government reforms to expand insurance access to both rural and urban residents, as well as increasing total health spending. In 2021, China ranked second worldwide in pharmaceutical sales, an impressive growth from the ninth position in 2005.

China’s pharmaceutical market has moved from a primary focus on generics manufacturing to the R&D of novel and innovative treatments. Fueled by favorable policies since 2017, new launches of innovative medicines have rapidly increased. China has also become one of the most important regions for global drug development due to its high potential growth. Sensing the immense commercial opportunity, big pharma foreign companies have followed the trend and secured some licensing deals with Chinese companies in recent years to further extend their market access for innovative drugs.

- **Japan**

In Japan, the Pharmaceuticals industry has experienced modest growth in recent years. Previously the second-largest pharmaceutical market after the U.S., Japan now ranked third, with China taking the second spot in recent years. An aging population and rising life expectancy have contributed to a strong demand for drugs and treatments, which would be a major driver of potential trends in the Pharmaceuticals industry in the region. However, based on IQVIA data, spending is expected to decline slightly through 2026 due to its annual price cuts. The Japanese pharmaceutical market is highly competitive, and many leading global pharmaceutical companies are based in Japan, including Takeda, Chugai, Daiichi Sankyo, and Eisai.

Operating Environment

Less Contribution from Covid-19 Related Sales Compared to Peak in 2021

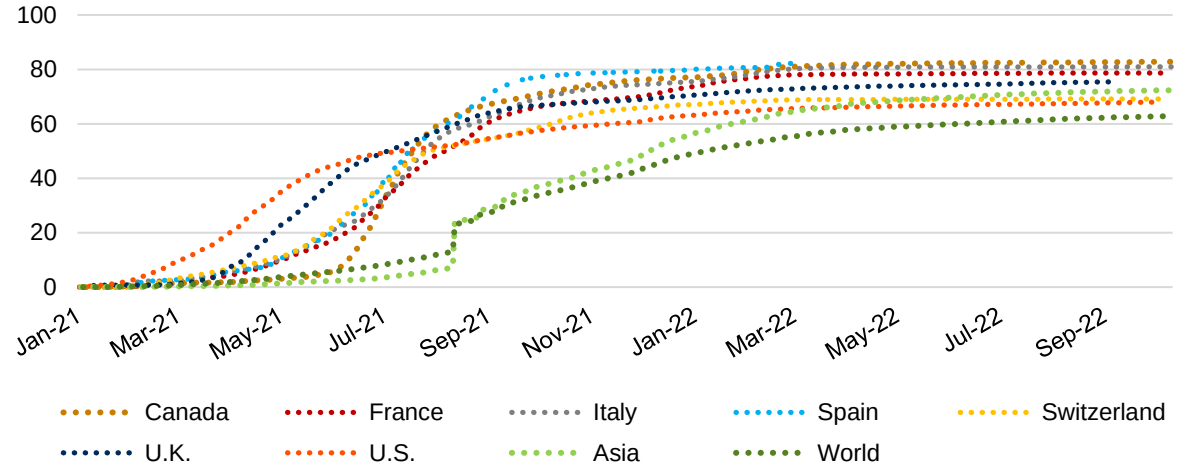
In 2021, Covid-19 vaccine frontrunners registered higher revenue from the contribution of Covid-19 vaccine sales, reaping the benefit of being the first movers in the Covid-19 vaccine market. AstraZeneca’s revenue grew by 41% year-over-year in 2021, but it was no match to the growth shown by Pfizer and Moderna, as AstraZeneca pledged to provide the vaccine at no profit during the pandemic. Pfizer’s sales nearly doubled to $81 billion in 2021, while Moderna’s sales shot to more than $18 billion in 2021 (versus $803 million in 2020).

Going forward, we expect to see less contribution from Covid-19 related sales amid improving health situation, particularly compared to the peak in 2021. Online data publication Our World in Data reported that more than 12 billion Covid-19 vaccine doses have been administered worldwide as of September 22, 2022, with 67.9% of the world population having received at least one dose of a Covid-19 vaccine, an improvement from 47.6% in October 2021. Many countries, especially the developed nations, started their Covid-19 inoculation drive since December 2020. As of September 2022, most developed countries such as the U.S. and major European countries have more than 50% of their populations vaccinated, while only 22.3% of people in low-income countries have received at least one dose (up from 14.5% in March 2022).

We note majority of companies that previously benefited from the surge in Covid-19 related products during the height of the pandemic are now guiding for lower or more stable Covid-19 related sales in 2022.

SHARE OF PEOPLE WHO COMPLETED THE INITIAL COVID-19 VACCINATION INITIAL PROTOCOL*

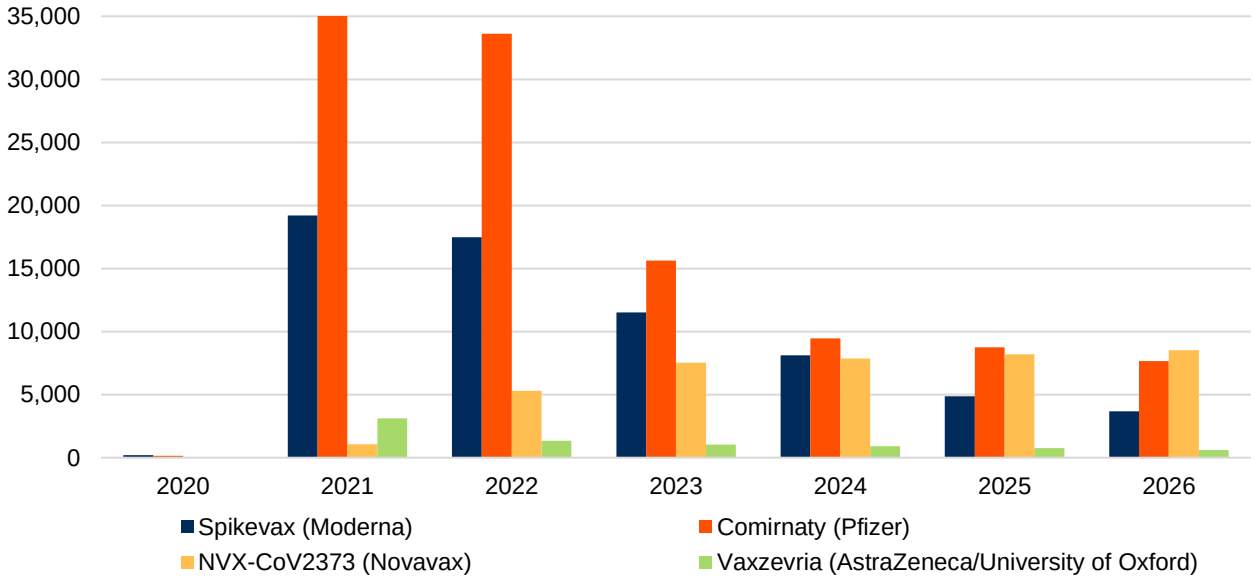
(percent)



*As of October 11, 2022.
Source: Our World in Data.

WORLDWIDE CONSENSUS FORECAST SALES: COVID-19 PROPHYLAXIS

($, millions)



Source: Evaluate.

Omicron (BA.5) Variant is Now Dominant in Most Countries

All viruses, including SARS-CoV-2 – the virus that causes Covid-19 – change over time. Some changes may affect the virus' properties, such as how easily it spreads and the associated disease severity. The higher number of Covid-19 cases has increased the risk of virus mutations, which leads to new variants. The emergence of new variants, in particular during late 2020, has prompted the characterization of specific Variants of Concern (VOCs) and Variants of Interest (VOIs) by the World Health Organization (WHO), in order to prioritize global monitoring and research.

VARIANTS OF CONCERN (VOC)*

WHO LABEL	EARLIEST DOCUMENTED SAMPLES	DATE OF DESIGNATION
Alpha	United Kingdom, September 2020	December 18, 2020
Beta	South Africa, May 2020	December 18, 2020
Gamma	Brazil, November 2020	January 11, 2021
Delta	India, October 2020	VOI: April 4, 2021 VOC: May 11, 2021
Omicron	Multiple countries, November 2021	VUM**: November 24, 2021 VOC: November 26, 2021

*A SARS-CoV-2 variant that meets the definition of a VOI and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- increase in transmissibility or detrimental change in Covid-19 epidemiology; OR
- increase in virulence or change in clinical disease presentation; OR
- decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

**Variants under monitoring (VUM): A SARS-CoV-2 variant with genetic changes that are suspected to affect virus characteristics with some indication that it may pose a future risk, but evidence of phenotypic or epidemiological impact is currently unclear, requiring enhanced monitoring and repeat assessment pending new evidence.

Source: WHO.

VARIANTS OF INTEREST (VOI)*

WHO LABEL	EARLIEST DOCUMENTED SAMPLES	DATE OF DESIGNATION
Lambda	Peru, December 2020	June 14, 2021
Mu	Colombia, January 2021	August 30, 2021

*A SARS-CoV-2 variant:

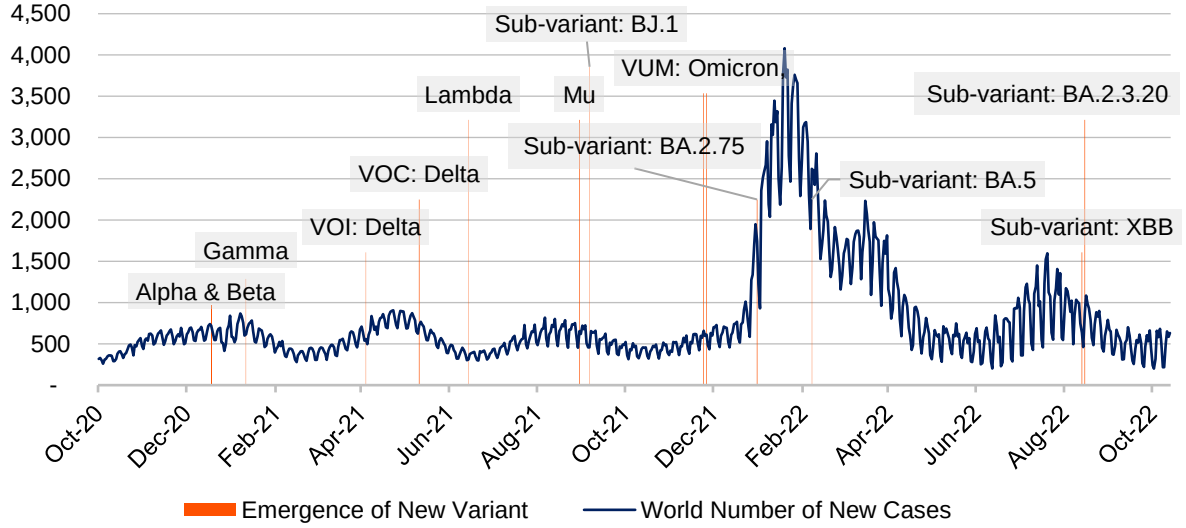
- with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- identified to cause significant community transmission or multiple Covid-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health.

Source: WHO.

After the Delta variant became dominant in several countries in mid-2021, Omicron has now surpassed it as the dominant variant since late 2021. Since the first two variants, Alpha and Beta, were discovered on December 18, 2020, the world has seen a fluctuation in the number of Covid-19 new cases. In mid-January 2022, the number of new cases spiked, reaching more than 4 million cases per day globally due to the Omicron wave impact. Despite several emergences of new Omicron sub-variants since February 2022, we observe a gradual decline in the trend of the number of new cases worldwide through October 2022 amid an increase in distribution of Covid-19 boosters worldwide.

TIMELINE OF EMERGENCE OF NEW VARIANTS VS. WORLD'S NUMBER OF NEW CASES*

(in thousands)



*As of October 13, 2022.
Source: Our World in Data, WHO.

Booster Shots and Covid-19 Drugs to Support Covid-19 Related Sales

Several vaccine developers have begun their studies and trials for booster shots of their vaccines amid concerns on the waning protection against Covid-19 infection and hospitalization over time, as well as the concern of the threat from new variants. Booster shots were first approved and recommended by regulators for the older age group as well as for those in the high risk group. The U.S. FDA first authorized a third dose of the Pfizer-BioNTech vaccine as a booster for people aged 65 and older, and other populations at high risk in September 2021, followed by the authorization of the Moderna booster (for people over the age of 65 and those with weakened immune system or greater risk of infection due to their work) and Johnson & Johnson booster (for adults aged 18 and older following primary vaccination with single-shot Johnson & Johnson vaccine; and for eligible individuals who received a different authorized Covid-19 vaccine) on October 20, 2021. Meanwhile, the European Medicines Agency (EMA) authorized a third dose of Pfizer-BioNTech and Moderna vaccines for people with severely weakened immune systems on October 4, 2021.

The approvals and recommendation were then extended to the other age groups. On October 12, 2022, the FDA granted approval for Moderna's and Pfizer's Bivalent Covid-19 vaccine for use as a booster dose in younger age groups. On September 1, 2022, the EMA's Committee for Medicinal Products for Human Use (CHMP) announced its recommendation of authorizing two vaccines adapted to provide broader protection against Covid-19. These vaccines consist of Comirnaty Original/Omicron BA.1 and Spikevax Bivalent Original/Omicron BA, which are intended for use in people aged 12 years and above who have received at least their primary vaccination against Covid-19. According to Our World in Data, 32.4 per 100 people have received booster doses (beyond the initial vaccination protocol) globally as of October 14, 2022.

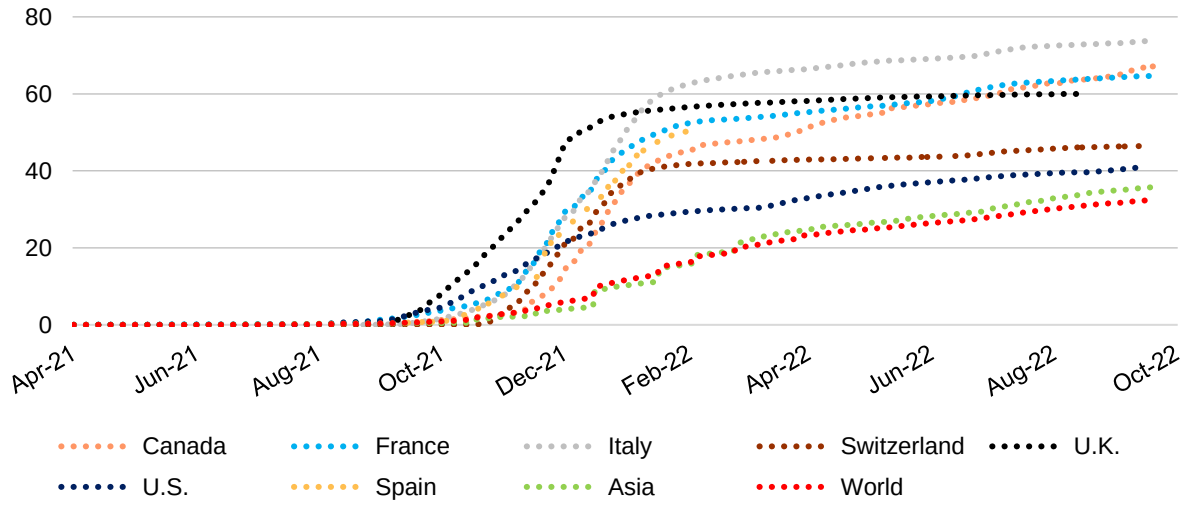
Studies of mixing Covid-19 vaccines when getting a booster shot were also conducted, which could open up the opportunity for other vaccine makers (besides the current frontrunners) in our view. Based on the studies, we note health regulators decided to allow the use of different vaccines for booster shots. The U.S. FDA announced the authorization of the use of heterologous ("mix and match") booster dose for currently available Covid-19 vaccines in October 2021 following a presentation of clinical trial data from the National Institute of Allergy and Infectious Disease, the Vaccines and Related Biological Products Advisory Committee's discussion of information submitted for consideration, and the FDA's evaluation of

the available data. The EMA followed suit after, announcing that a “mix-and-match” approach can be used for boosters.

Similarly, pharmaceutical companies are testing drugs and treatments for Covid-19. Covid-19 drugs that have been authorized by regulators include antiviral drugs Paxlovid (developed by Pfizer), Molnupiravir (Ridgeback Biotherapeutics and Merck & Co), and Remdesivir (Gilead Science), and antibody drugs Sotrovimab (GSK and Vir Biotechnology) and Evushled (AstraZeneca), following positive results in their respective clinical trials in reducing the risk of hospitalization or death caused by Covid-19. However, we note that since April 2022, Sotrovimab is no longer authorized to treat Covid-19 in any U.S. region due to the increasing proportion of Covid-19 cases caused by the Omicron BA.2 sub-variant (the dominant variant at the time) after data showed the authorized dose of Sotrovimab is unlikely to be effective against the said variant.

Overall, we expect booster shots as well as Covid-19 drugs and treatment to support Covid-19 related sales going forward, although not as significant as the primary vaccine. We reiterate our view of lower contribution from Covid-19 related sales going forward amid improving health situation.

COVID-19 VACCINE BOOSTERS ADMINISTERED PER 100 PEOPLE



*As of October 11, 2022.
Source: Our World in Data.

New Launches and Key Products are Back as Main Growth Drivers

With the anticipated dwindling Covid-19 related sales going forward amid improving health situation, we expect growth to be supported by key products and new launches. According to Evaluate Vantage, there are several projected product launches in 2022, with potential blockbuster status by 2026. These include Eli Lilly’s Donanemab, a drug to treat Alzheimer’s disease (although the company has deferred the timeline to complete the approval application later in 2022 from the first quarter of 2022), Roche’s Gantenerumab (for Alzheimer’s disease), Bristol Myers Squibb’s Deucravacitinib (for psoriasis and other autoimmune conditions) and Mavacamten (for cardiomyopathy), and Amgen/AstraZeneca’s Tezepelumab (for severe asthma).

BIGGEST POTENTIAL PRODUCT LAUNCHES IN 2022*

PROJECT	DESCRIPTION	COMPANIES	STATUS	2026 ESTIMATED SALES
Donanemab	Anti-amyloid-beta mAb for Alzheimer's disease	Eli Lilly	Phase III result expected to be reported in late 2022	$6.0 billion
Tirzepatide	GLP-1/GIP dual agonist for Type 2 diabetes, obesity	Eli Lilly	FDA approval granted in May 2022	$4.9 billion
Gantenerumab	Anti-amyloid-beta mAb for Alzheimer's disease	Roche	2022 launch assumes Roche files for U.S. accelerated approval	$2.5 billion
Deucravacitinib (BMS-986165)	TYK2 inhibitor for psoriasis, other autoimmune conditions	Bristol Myers Squibb	PDUFA September 10, 2022; EU approval expected Q4 2022	$2.4 billion
Bardoxolone	Nrf2 activator for rare, chronic kidney diseases	Reata	PDUFA February 25, 2022	$2.2 billion
Tezepelumab	Anti-TSLP mAb for severe asthma	Amgen/AstraZeneca	PDUFA Q1 2022; EU approval granted in September 2022	$2.0 billion
Vutrisiran	RNAi therapy for ATTR amyloidosis	Alnylam	PDUFA April 14, 2022; EU approval granted in September 2022	$1.8 billion
Mavacamten	Cardiac myosin inhibitor for cardiomyopathy	Bristol Myers Squibb	PDUFA April 28, 2022 (extended by 3 months); EU approval expected H2 2022	$1.7 billion
Cilta-cel	Anti-BCMA CAR-T for multiple myeloma	Johnson & Johnson	PDUFA February 28, 2022 (extended by 3 months); EU conditional approval granted in May 2022	$1.7 billion
Adagrasib	KRAS G12C inhibitor for lung cancer	Mirati Therapeutics	FDA targeted review date on December 14, 2022	$1.7 billion

*PDUFA = Prescription Drug User Fee Act.

Source: DCAT Value Chain Insights.

The Inflation Reduction Act

Rising drug prices are a big political issue in the U.S. Unlike other countries where governments directly or indirectly regulate prices, the U.S. leaves drug pricing to market competition, making it a very profitable market for pharmaceutical companies. U.S. spending on drugs was $580 billion in 2021 and has increased at a five-year CAGR of 3.5%, according to IQVIA.

Lowering drug prices continues to be a bipartisan issue in the U.S. as both the Democratic and Republican parties aim for more affordable drug prices for Americans. In August 2022, U.S. President Joe Biden signed into law the Inflation Reduction Act 2022, a package comprising health care, climate change, and taxation policy reforms. Among others, the Act allows the U.S. Department of Health and Human Services (HHS) to negotiate prices for certain high-cost Medicare covered drugs (including small molecule drugs and biologics) and to implement the negotiated prices starting in 2026 (starting initially with 10 Part D drugs and ramping up over time to 20 Part D or Part B drugs). HHS will select and publish the list of selected drugs for negotiation at least two years prior to the initial price applicability year – negotiation-eligible drugs will be selected from a list of Part D (retail prescription drugs) and Part B (administered by physicians) having the highest total expenditures. While it is not clear which drugs would be negotiated, we see those at the top end of the most expensive drug list to be at risk. Note that there are also other criteria such as the drugs must have been on the market for at least seven years as of the selection date for Part D (at least nine years for Part B) and the drugs that have generic or biosimilar competitor are excluded from the negotiation.

TOP 10 MEDICARE PART B SPENDING BY DRUG*
($, in billion of U.S. dollars)

BRAND NAME	GENERIC NAME	TOTAL SPENDING 2020
Keytruda	Pembrolizumab	3.5
Eylea	Aflibercept	3.0
Prolia	Denosumab	1.6
Opdivo	Nivolumab	1.6
Rituxan	Rituximab	1.3
Lucentis	Ranibizumab	1.1
Orencia	Abatacept	1.0
Neulasta	Pegfilgrastim	0.9
Darzalex	Daratumumab	0.8
Avastin	Bevacizumab	0.7

*Latest available data as of 2020.

Source: Centers for Medicare & Medicaid Services.

TOP 10 MEDICARE PART D SPENDING BY DRUG*
($, in billion of U.S. dollars)

BRAND NAME	GENERIC NAME	TOTAL SPENDING 2020
Eliquis	Apixaban	9.9
Revlimid	Lenalidomide	5.4
Xarelto	Rivaroxaban	4.7
Januvia	Sitagliptin Phosphate	3.9
Trulicity	Dulaglutide	3.3
Imbruvica	Ibrutinib	3.0
Lantus Solostar	Insulin Glargine,Hum.Rec.Anlog	2.7
Jardiance	Empagliflozin	2.4
Humira(Cf) Pen	Adalimumab	2.2
Ibrance	Palbociclib	2.1

*Latest available data as of 2020.

Source: Centers for Medicare & Medicaid Services.

Patent Expirations Expected to Peak in 2023 and 2025

Major patent expirations or “patent cliffs” are one of the major issues facing the Pharmaceuticals industry. Patent expirations for blockbuster drugs – those with global annual revenue exceeding $1 billion – are expected to peak in 2023 and 2025, including key patents like Stelara, which generates a significant amount of sales to Johnson & Johnson.

Despite the likely loss of revenue to patent owners, patent expirations would foster a more level playing field and are expected to reduce overall drug spending by about $141 billion through 2026, according to the “The Global Use of Medicines 2022: Outlook to 2026” report by IQVIA.

MAJOR POTENTIAL PATENT EXPIRATIONS
(arranged by patent expiry year)

PRODUCT	COMPANY	2022* SALES (in $, millions)	PHARMACOLOGICAL CLASS	MAJOR INDICATION
2023				
Stelara	Johnson & Johnson	4,887	Interleukin inhibitor	Psoriatic arthritis
2025				
Pomalyst	BMS	1,734	Immunomodulatory agent with antineoplastic activity	Multiple myeloma
Ofev	Boehringer Ingelheim	1,488	Tyrosine kinase inhibitor	Idiopathic pulmonary fibrosis
Xeljanz	Pfizer	802	Janus Kinase (JAK) inhibitor	Rheumatoid arthritis
Yervoy	BMS	1,040	Cytotoxic T-lymphocyte antigen 4 (CTLA-4)	Renal cell carcinoma (RCC)
2026				
Eliquis	Pfizer	3,537	Factor Xa inhibitor	Deep venous thrombosis (DVT)
2034				
Humira	AbbVie	10,099	TNF inhibitor	Psoriatic arthritis

Note: Patent expiration years are approximate for main indications in major markets (excluding line extensions and some already lost exclusivity), and are subject to change, depending on the success of generic entries.

*As of Q2 2022.

Source: Company reports.

Research & Development Environment

Patent expirations are usually followed by significant generic competition, which prompted large-cap branded pharmaceutical companies to spend on R&D in order to expedite pipeline cycle management of their existing blockbusters to be used in combination with new compounds. R&D spending by companies and the industry as a whole, as well as the number of new molecular entities (NMEs) or new active substance introduced (which have not been approved previously and frequently provide new therapies for patients), can be used as an important metric to show the level of R&D and competitive advantage of the industry.

According to Evaluate, global pharmaceutical R&D spending is expected to rise to $278 billion in 2026, growing at an annualized rate of 4.2% between 2021 and 2026, slightly lower than the historical CAGR of 4.7% between 2012 and 2020. The slower growth rate could be attributed to the use of big data analytics or artificial intelligence to enhance R&D processes, in our view.

As shown in the table below, Evaluate expects Roche will overtake Merck and Johnson & Johnson to be the biggest spender on pharmaceutical R&D (as a percentage of prescription drug sales) in 2026. Global spending on cancer (oncology) drugs is expected to continue as a primary driver of pharmaceutical spending growth. This spending is expected to reach $278 billion in 2026, according to Evaluate.

PHARMACEUTICAL RESEARCH & DEVELOPMENT (R&D) SPENDING

(ranked in terms of 2026 R&D expenditures, in billions of U.S. dollars)

RANK	COMPANY NAME	COUNTRY	PRODUCT FOCUS	R&D SPENDING		R&D AS A % OF PRESCRIPTION SALES	
				2022*	2026	2022(e)	2026
1	Roche	Switzerland	Pharmaceuticals (oncology, immunology, ophthalmology)	6.6	16.9	27.8	28.7
2	Merck & Co	U.S.	Pharmaceuticals (oncology), animal health	5.4	12.8	21.4	23.1
3	Johnson & Johnson	U.S.	Consumer products, medical devices	7.2	12.3	22.5	21.5
4	AstraZeneca	U.K.	Pharmaceuticals (cardiovascular, oncology, respiratory)	4.7	11.2	21.5	21.2
5	Bristol Myers Squibb	U.S.	Pharmaceuticals (oncology, immunology)	4.6	10.1	20.4	20.3
6	Novartis	Switzerland	Pharmaceuticals (oncology), generics	4.8	10.0	17.8	17.8
7	Eli Lilly	U.S.	Pharmaceuticals (diabetes, oncology)	3.4	9.0	30.9	25.9
8	Pfizer	U.S.	Pharmaceuticals (diabetes, hemophilia)	5.1	8.7	9.0	13.7
9	GSK	U.K.	Pharmaceuticals (respiratory, HIV), vaccines	2.2	8.1	20.2	19.9
10	AbbVie	U.S.	Pharmaceuticals (oncology, immunology, neuroscience)	3.1	7.6	12.2	13.3

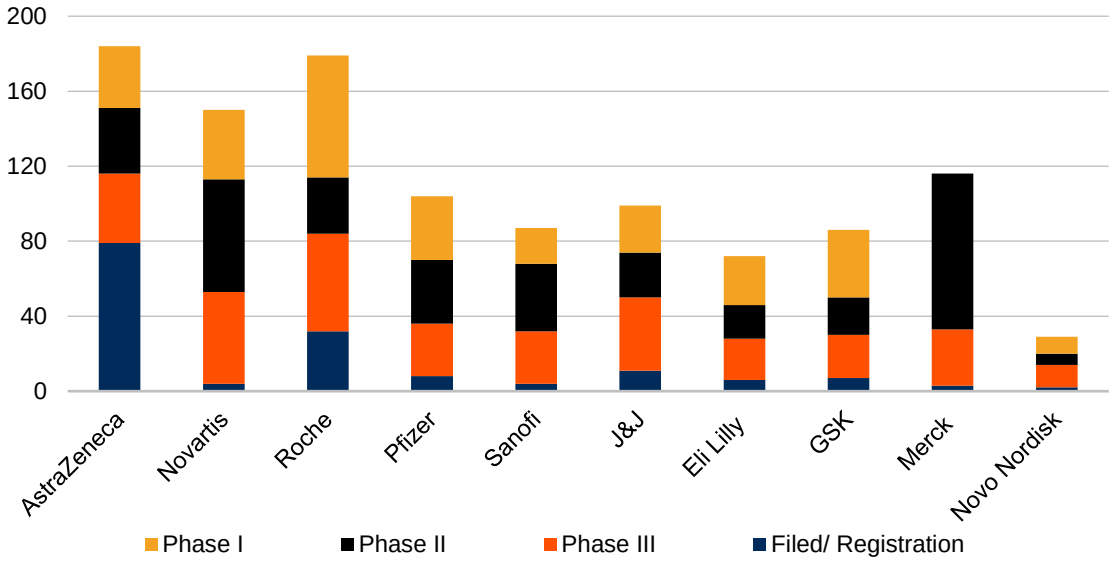
*As of Q2 2022.

Source: Evaluate, Company Reports.

The graph on the next page shows the R&D pipeline for the top 10 global pharmaceutical companies. As of July 2022, we note that AstraZeneca has the highest Phase III and filed/registration pipeline of 116, followed by Roche at 84 and Novartis at 53. In our view, having a large R&D pipeline, particularly the late-stage pipeline (Phase III and filed/registration), is vital to support future revenues and could help pharmaceutical companies offset some patent losses.

RESEARCH AND DEVELOPMENT PIPELINE BY PHASE I, II, III, AND FILED/REGISTRATION FOR TOP 10 GLOBAL PHARMACEUTICAL COMPANIES*

(number of pipelines)



*Data as of July 2022.
Source: CFRA, Company Filings.

The Potential of Cell, Gene, and RNA Therapies

Cell therapy aims to treat diseases by restoring/altering certain sets of cells or by using cells to carry a therapy through the body. With cell therapy, cells are cultivated or modified outside the body before being injected into the patient. Gene therapy aims to treat diseases by replacing, inactivating, or introducing genes into cells – either inside the body (in vivo) or outside the body (ex vivo). Some therapies are considered both cell and gene therapies, which work by altering genes in specific types of cells and inserting them into the body.

After several setbacks over the last couple of decades, cell, gene, and RNA-based therapies are starting to make significant progress, with new therapies being developed across various therapeutic areas. According to IQVIA, 30 cell, gene, or RNA-based therapies have launched globally as of November 2021, with additional 55-65 therapies anticipated to be launched by 2026. The total global spending as of November 2021 reached $5 billion and is estimated to increase to $20 billion by 2026, although with significant uncertain clinical and commercial successes. IQVIA expects the estimated spending to be dominated by cell and RNA therapies and will be slightly less contributed by gene therapy. This marks a substantial growth compared to the first therapies that were launched in 2010, which had less than $1 billion total spending until 2018. Nevertheless, these new therapies are expected to encounter some challenges in the industry such as market access limitations across geographies, with spending and usage mostly limited to major developed markets. More limited reimbursement could potentially lead to lower uptake, resulting in lower levels or delayed usage and spending across these areas. Several other uncertainties include potential improved performance of already marketed therapies and ambiguous outcomes on ongoing research.

The concern over the safety of gene therapy has once again been brought to attention when Novartis recorded two deaths after treatment with its spinal muscular atrophy gene therapy, Zolgensma, in August 2022. Two children died of acute liver failure, a known side effect of Zolgensma, about five to six weeks after receiving the therapy. While severe liver injury is a notable risk of Zolgensma, the two deaths are the first reports of fatal cases. Novartis highlighted that it would notify regulators including the FDA to update Zolgensma's labeling to specify the fatal acute liver failure reports.

China embraced its clinical trial of gene therapy in 1990 and approved the world's first gene therapy product in 2003 – Gendicine, a gene therapy product developed by Shenzhen Sibiono Genetech for the treatment of head and neck cancer. Between 2009 and 2019, the Chinese government, led by the National Health Commission and the NMPA, released a series of progressive policies to strengthen regulations in the gene therapy sector to protect intellectual property. For example, in September 2019, the State Council of the People's Republic of China restricted any genetic information to be transferred abroad, and health data can be viewed remotely but must be stored on a local server in China. Driven by strong policy support, China has already become a hub for gene therapy development, with more than 45 local companies with Investigational New Drug-approved pipelines.

In 2017, the U.S. FDA approved Luxturna (developed by Spark Therapeutics, one of the first FDA-approved in vivo gene therapy) for the treatment of any heritable retinal dystrophy caused by the mutated RPE65 gene. The U.S. FDA also approved Kymriah, a chimeric antigen receptor (CAR) T cell therapy by Novartis for the treatment of acute lymphoblastic leukemia (ALL). CAR-T cell therapy works by programming a patient's immune cell to recognize and target cells with cancerous mutations.

There have been other approvals since Luxturna and Kymriah, including Zolgensma, a one-time infusion to treat infants with spinal muscular atrophy, which received conditional marketing authorization in May 2020. There are over 1,000 gene therapy clinical trials in the pipeline, with the U.S. FDA and the EMA predicting they will each approve 10 to 20 cell and gene therapies per year by 2025.

Demographics Shape Pharmaceutical Consumption

The worldwide demographic trends that bode well for long-term pharmaceutical consumption are the aging of the population in the largest markets, the lengthening of the average life expectancy, and a rising incidence of chronic diseases. In many countries, the elderly population – a group with disproportionately greater use of prescription drugs – is growing faster than the general population.

The share of world population aged 65 years or over increased to 10% in 2021 and is projected to increase further to 16% by 2050, according to "World Population Prospects 2022" by the United Nations. In the U.S., the Census Department projected that the 65-and-older segment of the population will grow to 94.7 million in 2060 from more than 54 million in 2019 (latest available). In Europe, the European Commission projected the number of elderly persons (65 and older) to increase to 129.8 million in 2050 from 90.5 million at the start of 2019 (latest available). In Japan, the National Institute of Population and Social Security Research estimated that the old-age population will increase to 39 million in 2042, from 36.2 million in 2020 (latest available). China's elderly population is anticipated to double over the next two decades, which will put increasing pressure on the country's health care system, in our view.

Companion Animal Health Trend in the U.S.

New pet ownership has remained high in the U.S. since the Covid-19 pandemic. As people have been spending more time at home, in 2020 (latest available), pet ownership in the U.S. increased to 70% (about 90.5 million families) of households vs. 67% earlier (roughly 85 million families), reaching an all-time record based on American Pet Products Association (APPA) 2021-2022 National Pet Owners Survey. Total U.S. pet expenditure grew 6.7%, reaching $103 billion in 2020 (latest available) compared to the previous year despite the onset of the Covid-19 pandemic in the U.S. in March 2020.

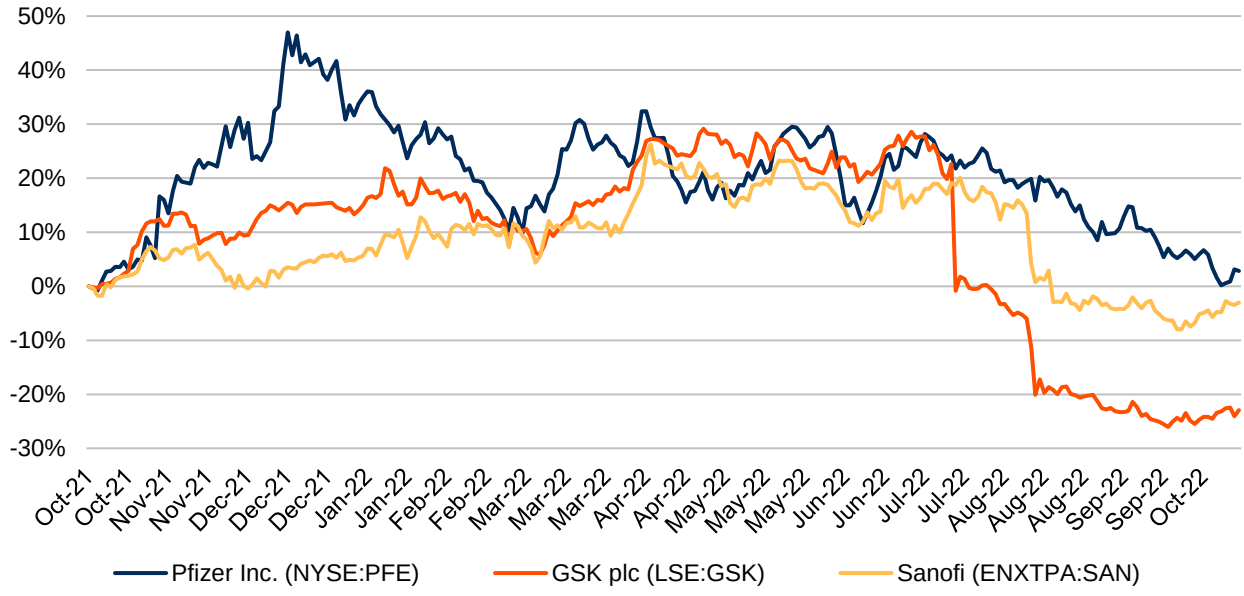
In our view, Zoetis, which is the global leader in Animal Health, and Merck, which generates 11% of its revenue from Animal Health ($5.6 billion in sales in 2021), are well-positioned to absorb the growing demand in Animal Health thanks to their diverse portfolio of animal medicines, vaccines, and vitamins. In 2021, Zoetis's Companion Animal revenue grew by 27% year-over-year, which cushioned just 1% revenue growth in the Livestock segment. Although Animal Health makes up only 11% of Merck's total business, it was one of the company's most resilient segments during 2021, when other segments were hard hit by the Covid-19 pandemic. Companion Animal made up 41% of Merck's Animal Health revenues in 2020, generating $2.3 billion in revenue, despite Covid-19 related business disruptions.

Litigation Risk Impacting Share Price Performance

In August 2022, share prices of several pharmaceutical companies including Sanofi and GSK were impacted by the concern over Zantac's (heartburn drug) litigation risk (claims alleging the drug causes cancer). Class actions and personal injury lawsuits were filed after the U.S. FDA raised safety concerns in 2019. Zantac was originally developed by GSK and was launched back in 1983. Sanofi acquired the over-the-counter (OTC) rights to Zantac in 2017. Before that, there were other companies that marketed prescription and/or branded OTC Zantac over time including Pfizer and Boehringer Ingelheim – which are also named as defendants in these actions. Given Zantax's rights were held by different companies at various times, potential liability may also be split among these players, in our view.

We note a plaintiff in Illinois whose case was scheduled to be the first Zantac trial had voluntarily dismissed his case. In a statement released on August 16, 2022, GSK said it did not settle the pliantiff's claim and will continue to "vigorously defend all claims". According to GSK, among the state court cases naming GSK, a trial in California and a trial in Madison County, Illinois, are currently scheduled to begin in February 2023. Sanofi, via company's statement, also said the first trial that may involve Sanofi as a defendant is currently scheduled for February 2023 as a part of California state court proceedings.

SHARE PRICE PERFORMANCE*



*Data as of October 17, 2022.
Source: S&P Global Market Intelligence.

TOP 10 LARGEST SETTLEMENTS BY PHARMA COMPANIES

COMPANIES	DESCRIPTION	SETTLEMENT AMOUNT	STATUS
Purdue Pharma	Deceptive marketing campaign that minimized health risks of opioids and claimed that prescription drugs were rarely the cause of abuse, addiction, or death	$6 billion	Ongoing
Merck & Co.	Arthritis pain drug Vioxx was pulled from the market over safety concerns and several product liability trials	$4.85 billion	Completed in 2007
American Home Products Corp. (now Wyeth)	Weight-loss combination known as “fen-phen” was pulled from the market due to serious, potentially fatal heart valve problems	$3.75 billion	Completed in 2000
GSK	Promoted drugs such as antidepressants, Paxil and Wellbutrin, for unapproved uses, failure to provide safety data for Avandia diabetes drug, and for paying kickback to doctors	$3 billion	Completed in 2012
Pfizer	Improper marketing for 13 drugs for unapproved uses	$2.3 billion	Completed in 2009
Takeda	Type 2 diabetes drug Actos caused bladder cancer	$2.3 billion	Completed in 2015
Johnson & Johnson	Promoted antipsychotic drugs Risperdal and Invega for unapproved uses and for paying kickback to pharmacists	$2.2 billion	Completed in 2013
Abbott Laboratories	Promoted anti-seizure drug Depakote for unapproved uses	$1.6 billion	Completed in 2012
Eli Lilly	Promoted top-selling schizophrenia drug Zyprexa for unapproved uses	$1.42 billion	Completed in 2009
Reckitt Benckiser	Carried out illegal scheme to boost sales of an opioid addiction treatment	$1.4 billion	Completed in 2019

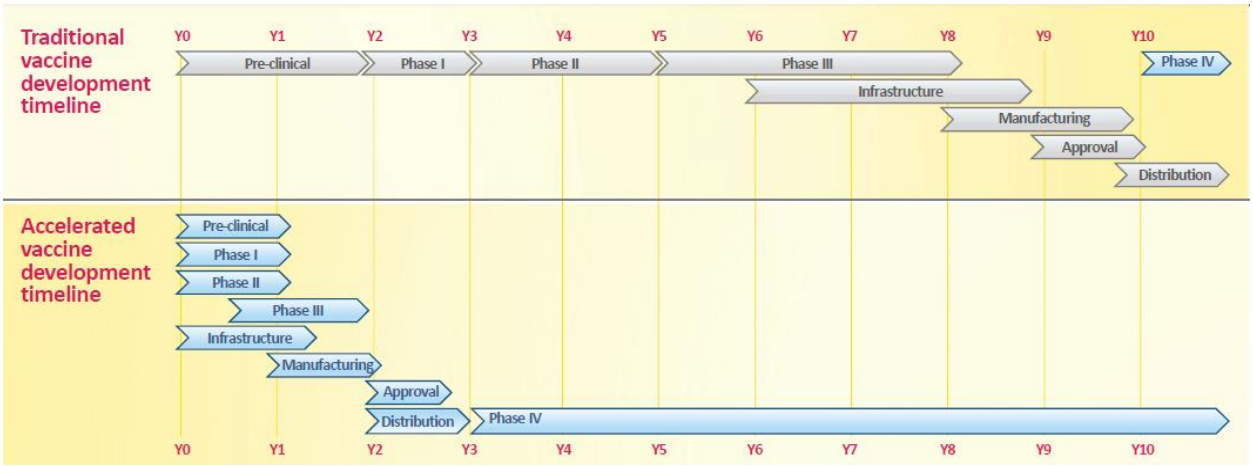
Source: Fierce Pharma, Reuters, DoJ.

Regulatory Updates

Fast Track Approval Process for Potential Covid-19 Vaccine and Treatment
The rapid spread of Covid-19 globally since March 2020 has caused health care authorities to fast-track the review of vaccines and treatments that might be used to fight the pandemic. The traditional vaccine development could take up to 10 years from the pre-clinical phase to distribution as each step is performed in sequence. To accelerate Covid-19 vaccine development, these steps have been done in parallel, which could cut the timeline down to two to three years (from pre-clinical to distribution).

For example, the U.S. FDA established the Coronavirus Treatment Acceleration Program (CTAP) to expedite the availability of new treatments and vaccines for Covid-19 patients. The program uses every available method to move new treatments to patients as quickly as possible and ensures that the safety and effectiveness of these treatments and vaccines are simultaneously evaluated.

On the other hand, the EMA announced that it would accelerate regulatory procedures to support the development and regulatory approval for treatment and vaccines for Covid-19. A “rolling” review allows the EMA to expedite the evaluation procedures and look at how the vaccine performs in real time as data emerge from trials instead of waiting for the drug companies to submit everything at once. Once the EMA has enough information to make a decision, the drug companies will submit a formal application.



Source: WHO.

OECD Deal Imposes Global Minimum Taxation
On October 8, 2021, the OECD unveiled its October 8 Landmark Agreement to promote fairer international tax arrangements and was backed by 136 countries + Mauritania. The two-pillar solution agreement consists of Pillar One and Pillar Two.

Pillar One outlines taxing rights of over 25% of the residual profit of the largest multinational enterprises (MNEs), and the most profitable MNEs (more than $125 billion) are expected to be reallocated to market jurisdictions every year. Pillar Two introduces a global minimum taxation of at least 15% on multinationals with more than $835 million in annual revenue and estimated additional global annual tax revenue of $150 billion.

The new taxation is scheduled to take effect in 2023, and we foresee that this would potentially hurt the bottom-line profitability of large multinational pharmaceuticals that generate more than 50% of their sales internationally.

UNITED STATES

Potential Negative Impact of Increased Taxation on U.S. Pharmaceuticals

President Biden plans to double the current tax rate of foreign profits of U.S. firms, aiming to bring higher tax revenues to the U.S. President Biden also aims to end tax breaks given to U.S. firms investing abroad.

EUROPEAN UNION

Clinical Trials Regulation

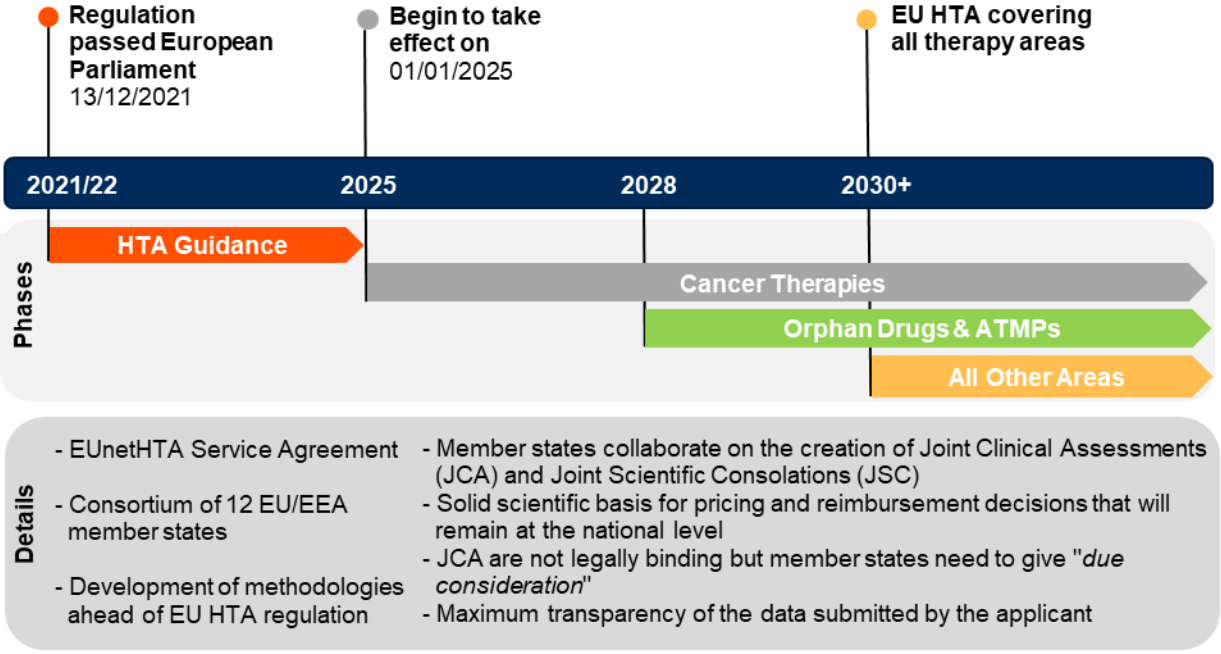
Clinical Trials Regulation (CTR), which aims to harmonize the process for assessment and supervision of clinical trials throughout the EU, entered into application on January 31, 2022. CTR repealed the previous Clinical Trials Directive (CTD). CTR enables sponsors to submit one online application via a single online platform known as the Clinical Trials Information System (CTIS) for approval to run a clinical trial in several European countries, making it more efficient to carry out such multinational trials. This also makes it more efficient for the EU Member States to evaluate and authorize such applications together via CTIS. Prior to CTR, clinical trial sponsors had to submit clinical trial applications separately to national competent authorities and ethics committees in each country to gain regulatory approval to run a clinical trial. Under CTR, national regulators in the EU Member States and European Economic Area (EEA) countries have started using CTIS from January 31, 2022, while clinical trial sponsors have a three-year transition period: (i) until January 31, 2023, clinical trial sponsors may use CTIS to apply to run clinical trials under CTR or may choose to apply to run trials under CTD; (ii) from January 31, 2023, clinical trial sponsors will need to use CTIS to apply to start a new clinical trial in the EU and EEA; (iii) from January 31, 2025, any trials approved under CTD that continue running will need to comply with the CTR and their sponsors must have recorded information on them in CTIS.

Regulation on Health Technology Assessment

The Regulation on Health Technology Assessment (HTA), billed as a key deliverable of the European Pharmaceutical Strategy, was adopted in December 2021 in the EU. The Regulation will apply from January 2025, but the implementation work starts now, including the setting up of the necessary governance structure and preparatory documents to ensure effective application from this date. The Regulation supersedes the current system of EU-funded project-based cooperation between Member States on HTA by introducing a permanent framework for joint work that will also cover joint scientific consultations, the identification of emerging health technologies, and voluntary cooperation, as well as work on joint clinical assessments.

EU PROPOSES HARMONIZED REGULATION ON HTA IN PHASED APPROACH, STARTING WITH CANCER THERAPIES IN 2025

Aim to improve medicine availability, ensure efficient resource usage and strengthen HTA quality



Source: IQVIA.

CHINA

Key Tasks for Deepening the Reform of Medical and Health System

In May 2022, China's General Office of the State Council issued the "Key Tasks for Deepening the Reform of Medical Health System in 2022", which clearly defined the road map for the reform. Through a series of measures, such as expanding the scope of Volume-Based Procurement (VBP) of pharmaceuticals and consumables, reforming the prices of medical services, reforming the payment methods of medical insurance, and strengthening comprehensive supervision, China's government aims to deepen the integrated reform of medical care, medical insurance, and medicine, so as to continuously promote the prices of pharmaceuticals and consumables to return to a reasonable level, to reform pharmaceutical distribution supply chain, and to accelerate the expansion and balanced distribution of high-quality medical resources.

China's 2021 National Reimbursement Drug List

On December 3, 2021, the National Healthcare Security Administration (NHSA), the current payer of China's public health security system, published the 2021 National Reimbursement Drug List (NRDL). The finalized 2021 NRDL, which came into effect on January 1, 2022, now comprises a total of 2,860 drugs, of which 1,486 consist of Western-made medicines and 1,374 Chinese-patented medicines. On average, pharmaceutical companies agreed to cut drug prices by 61.7% to gain access to the list, on par with 50.6% price fall in 2020. China has updated the NRDL annually since 2017, with the price negotiation mechanism regularly resulting in substantial price cuts to marketed drugs. As a comparison, the average drug price reduction was 61% in 2019, 57% in 2018, and 44% in 2017. Drugs developed by foreign pharmaceutical companies also have an equal chance to participate in the price negotiation process in order to launch their products in the Chinese market. Some key drugs developed by foreign companies that made the 2021 NRDL list include Pfizer's Vyndamax, Takeda's Fabry's disease treatment Replagal, and Takeda's Firazyr.

JAPAN

Measures to Control Increasing Drug Prices

As spending on pharmaceutical products continues to accelerate in Japan, the government has started to implement and explore ways to control the surging costs of drugs for maintaining the health of its aging population. Japan conducts regular price revision every two years in April, with the latest price revision conducted in April 2021. In December 2016, the Japanese government decided to conduct additional price revisions in between the regular biennial price revisions ("off-cycle" price revisions). The targets of these "off-cycle" price revisions are products with large price discrepancies (i.e., gaps between the listed price and market price). The first "off-cycle" price revision was conducted in April 2021.

M&A Environment

Focusing on Core Businesses

Merger and acquisition (M&A) activity for global pharmaceuticals is holding up well so far in 2022. To date through October 2022, the industry saw the conclusion of the $1.9 billion deal of UCB's acquisition of Zogenix Inc (on March 4, 2022) and CSL Behring's acquisition of Vifor Pharma. Novo Nordisk also announced the proposed acquisition of Forma Therapeutics, a clinical-stage company focusing on sickle cell disease and rare blood disorder, which is targeted to close in the fourth quarter of 2022.

We also note the continuous trend in companies' efforts to focus on core businesses, with several announcements of spinning off or strategic review of non-core segments over the years. In June 2021, Merck spun off its women's health, legacy brands, and biosimilars businesses into a new company, Organon, while GSK has successfully completed the demerger of its Consumer Healthcare business in July 2022. The "new GSK" now consists of Pharmaceuticals and Vaccines businesses. Novartis also announced its intention to separate its generic arm Sandoz into a new publicly traded standalone company, by way of a 100% spin-off. Sandoz has been a drag on the company's overall performances over the years, as the unit continues to be impacted by pricing pressure. The spin-off is expected to be completed in the second half of 2023, subject to shareholders' approval as well as the general market condition.

2022 could see an improvement in M&A activity compared to 2021, although the recent announcement by the Federal Trade Commission (FTC), regarding a major review of how it has handled M&A in pharmaceutical and biotech industry, could increase the scrutiny on potential M&A deals in the industry. CFRA thinks vaccines and treatments connected to Covid-19 response will likely create opportunities for specialist drug discovery companies to become targets for acquisitions. Meanwhile, we also expect large pharmaceutical companies to continue to divest non-core assets to focus on high-growth businesses.

GLOBAL PHARMACEUTICAL M&A ACTIVITY IN 2020 - 2022

(deals of at least $1 billion, as of October 31, 2022)

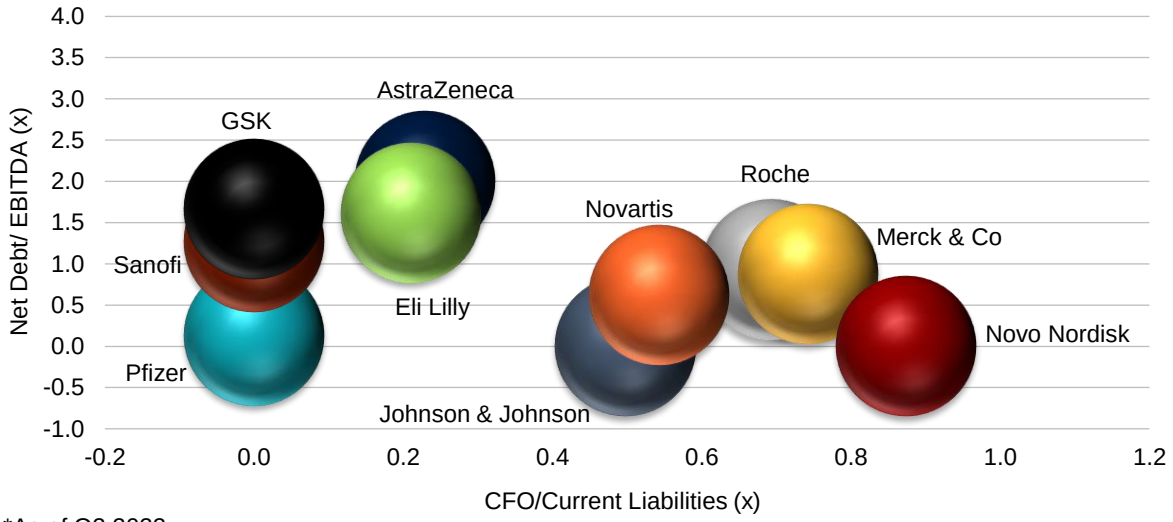
DATE ANNOUNCED	BUYER	COUNTRY OF BUYER	TARGET	COUNTRY OF TARGET	TRANSACTION VALUE ($, billions)	TRANSACTION STATUS	DATE CLOSED
08/04/2022	Amgen	U.S.	ChemoCentryx	U.S.	4.0	Closed	10/20/2022
09/01/2022	Novo Nordisk	Denmark	Forma Therapeutics	U.S.	1.1	Closed	10/14/2022
08/08/2022	Pfizer	U.S.	Global Blood Therapeutics	U.S.	5.6	Closed	10/05/2022
05/10/2022	Pfizer	U.S.	Biohaven Pharmaceutical	U.S.	12.2	Closed	10/03/2022
05/31/2022	GSK	U.K.	Affinivax	U.S.	3.3	Closed	08/16/2022
06/03/2022	Bristol-Myers Squibb	U.S.	Turning Point Therapeutics	U.S.	4.0	Closed	08/15/2022
08/04/2022	Amgen	U.S.	ChemoCentryx	U.S.	4.0	Closed	10/20/2022
7/5/2022	AstraZeneca	U.S.	TeneoTwo	U.K.	1.3	Closed	8/11/2022
1/19/2022	UCB	Belgium	Zogenix	U.S.	1.9	Closed	3/4/2022
12/14/2021	CSL	Australia	Vifor Pharma AG	Switzerland	12.8	Closed	8/9/2022
9/8/2021	Perrigo Company	Ireland	HRA Pharma, SA	France	2.1	Closed	4/29/2022
7/9/2021	PMI Global Services	U.S.	Vectura Group	U.K.	1.4	Closed	10/19/2021
5/10/2021	Trulieve Cannabis	U.S.	Harvest Health & Recreation	U.S.	2.3	Closed	10/1/2021
12/14/2020	EQT Partners	Sweden	Recipharm AB	Sweden	3.5	Closed	3/1/2021
12/12/2020	AstraZeneca	U.K.	Alexion Pharmaceuticals	U.S.	39.0	Closed	7/21/2021
11/6/2020	Novo Nordisk	Denmark	Emisphere Technologies	U.S.	1.3	Closed	12/8/2020
10/5/2020	Bristol Myers Squibb	U.S.	MyoKardia	U.S.	13.1	Closed	11/16/2020
8/24/2020	Oscar A-Co KK	Japan	Takeda Consumer Healthcare	Japan	2.3	Closed	3/31/2021
8/19/2020	Johnson & Johnson	U.S.	Momenta Pharmaceuticals	U.S.	6.4	Closed	9/30/2020
8/17/2020	Sanofi	France	Principia Biopharma	U.S.	3.7	Closed	9/25/2020
6/11/2020	Novo Nordisk	Denmark	Corvidia Therapeutics	U.S.	2.1	Closed	7/31/2020
5/26/2020	Merck & Co.	U.S.	Themis Bioscience	Austria	1.1	Closed	6/19/2020
1/10/2020	Eli Lilly and Co.	U.S.	Dermira, Inc.	U.S.	1.3	Closed	2/19/2020

Source: CFRA, S&P Global Market Intelligence.

A Solid Balance Sheet is Key to Support Any Inorganic Expansion

Below, we illustrate the net debt to EBITDA ratio and cash flow from operation to current liabilities ratio (CFO to current liabilities) for the top 10 global pharmaceutical companies. Based on our analysis, Novo Nordisk, Merck & Co, and Roche have better balance sheet positions relative to others (higher CFO to current liabilities and lower net debt to EBITDA ratio), which could indicate their better capability to support M&A activities.

GEARING RATIO AND DEBT COVERAGE FOR TOP 10 GLOBAL PHARMACEUTICAL COMPANIES, 2022*



*As of Q2 2022.
Source: CFRA, S&P Global Market Intelligence.

HOW THE INDUSTRY OPERATES

High Risk, High Rewards
Drug manufacturing is a high-risk business: for every 5,000 compounds discovered, only one reaches the pharmacist's shelf. The odds against making a profit are steep as well: fewer than a third of marketed drugs achieve enough commercial success to recoup their R&D investments. However, when a drug maker launches a new compound that is widely accepted in the marketplace, the economic rewards can be immense. This is the primary reason for the industry's hefty profit margins.

Predictable Life Cycles of Drugs
Drugs have widely different development processes, but the product life cycle nearly always follows a stable, long-term pattern; which begins with drug discovery and includes development, testing, approval, production, as well as post-marketing survey. The cycle for discovery, development, testing, and approval could take up to 10 years or more on average.

Drugs often require several years of sales build-up to reach their full commercial potential. Physicians have to become comfortable with the product and its approved application, while companies often continue conducting clinical trials that will enable them to receive regulatory approval for additional indications.

In some cases, companies benefit as doctors start to use their drugs for off-label (or unapproved) indications; these sometimes represent a hefty proportion of a drug's total revenues. Eventually, rival drugs similar in action may enter the market, or major customers may opt to replace the drug with less expensive compounds in the same therapeutic class. The latter tactic, referred to as "therapeutic substitution", is especially popular with managed care companies.

Source: Happiest Minds Technologies.

How New Drugs Enter the Market

Regulators require that pharmaceutical manufacturers perform extensive testing to prove that their products are safe and effective before the regulators will sanction commercial sale. All animal and human tests, which often last for years and cost many millions of dollars, are conducted by manufacturers, often in conjunction with colleges or universities, the National Institutes of Health, or similar research institutions.

Identifying and Testing Candidate Drugs
A drug lifecycle begins with drug discovery. Drug makers usually spend large sums on R&D in order to produce a steady stream of successful products. Research for innovative products is especially challenging in the Pharmaceuticals industry, because products come from highly complex fields, such as molecular biology and biochemistry, and involve the intricate workings of the human body. The quest for new pharmaceuticals must combine an understanding of complex human chemistry and physiology with knowledge of all life sciences.

Working from a set of hypotheses on how certain compounds might interact in the body, researchers synthesize new compounds to combat particular diseases. Proteins, segments of proteins, genes

(isolated by molecular biologists), or new chemicals (discovered by analytical chemists) are often the basis of new drugs.

Once candidate molecules are identified, they are studied in test tubes and in animals to determine their side effects, efficacy, and properties (such as how long the body takes to absorb them). Animal tests (usually on mice and rats) are conducted to determine any possible side effects and efficacy. Most new drug candidates are eliminated at this stage because they have unacceptable side effects or do not function as expected. Often, hundreds of compounds are tested before researchers find one promising enough to advance to human clinical trials. Clinical trials happen in several phases during which different questions are asked. Each phase builds on the results of previous phases.

Below are the examples of the clinical trial phases:

◆ **Phase I.** In this phase, a small number of healthy people get moderate doses of the drug to test the drug's safety, safe dosing range, and mechanism of action. If this initial test is successful, the subjects' dosage is slowly increased to determine its safety at higher levels.

◆ **Phase II.** During Phase II, a larger group of subjects with the disease or condition that the drug is intended to treat is tested in placebo-controlled clinical trials. Phase II researchers look for efficacy and continue to study safety and optimal dosing.

◆ **Phase III.** Drugs that pass the first two hurdles then undergo Phase III trials. At this level, the most complex and rigorous tests are performed on still larger groups of ill patients to ascertain the drug's safety, effectiveness, and optimum dosage regimens. Usually, Phase III procedures employ randomized, double-blind studies with placebo control. This means that one group of patients is given the drug while another group receives an inert substance. Neither the patients nor their doctors are aware of which patients are actually receiving the drug being tested.

◆ **Phase IV.** In this phase, which is also known as "post marketing trial", the drug is tested after drug approval or when it is launched in the market. Trials are carried out after country approves the drug for commercial purpose and is studied to evaluate the need for further testing in a wide population over a longer time frame. Investigators use this phase to get more information about the drug's long-term safety, effectiveness, and any other benefits.

Approvals and Production

When the clinical research on a drug is complete, the manufacturer submits application to respective regulatory bodies for drug approval. For example, in the U.S., a drug manufacturer will submit Marketing Authorization Approval (MAA)/New Drug Application (NDA) to the FDA in order to manufacture and sell the drug in the country. The application compiles the research completed during the three trial phases and includes full details of the product's formula, production, labeling, and intended use.

After a drug is approved, manufacturers often submit supplemental NDAs containing additional clinical trial results, in order to obtain approval for additional indications. The FDA determines label content, which must include a detailed description of the drug and its chemical composition, indications, contraindications, and side effects.

The Pharmaceuticals industry is global; thus, a company seeking to maximize a drug's potential files for its approval in many countries. Companies can apply to NMPA for approval in China and to PDMA for approval in Japan. Companies filing for regulatory approval in the EU can either apply through a centralized EU procedure that enables them to sell their approved products in all EU countries, or file on an individual country basis. The Amsterdam-based EMA reviews all applications submitted under the centralized process and recommends them to the European Commission, which grants final marketing authorization. The alternative, known as the "mutual recognition" procedure, allows drug makers with a medicinal product already approved in one EU country to petition other countries to accept the product. Should an EU country refuse to recognize the original country's authorization, the matter is submitted to an EMA scientific committee for arbitration.

Production of a drug can be started once the drug is authorized for marketing. Manufacturers procure the quality raw material/substance with defined ingredients and quality equipment meeting regulatory requirements required to manufacture the drug. Good manufacturing practice (GMP, a system for ensuring that products are consistently produced and controlled according to quality standards) should be followed throughout the drug manufacturing phase. Post-production, marketing of the drug is an essential part of the lifecycle. The labeling should clearly give instruction about storage and transportation, and the distribution should be made region-wise with compliance of the local governing authorities.

Patents and Exclusivity Rights

A patent is a temporary monopoly granted to an inventor by law, which prevents others from exploiting the invention (*i.e.,* manufacturing, selling, or importing the invention). Inventors are required to disclose the patent specification of their invention in order to seek the legal scope of the monopoly through the claims of the patent specification. The term of the monopoly is usually 15 to 20 years, depending on the country. To be patentable, an invention should be novel, inventive (not obvious), and capable of industrial application. U.S. patent law permits the granting of a patent on a composition of matter, such as a novel type of concrete or new molecule, and new and useful improvement of the molecule.

In most of the countries where patent law exists, the degree to which these conditions are applied varies. The patent application is published 18 months from the priority date of the invention. Because a patent protects an invention only in the country where granted, inventors must file a patent application in all countries where patent protection is required. The initial application establishes the priority date (the date from which the invention is considered novel). Inventors have 12 months to file corresponding patent applications based on the original priority date in the member countries of the Paris convention, which allows patent families the equivalent invention in different countries.

Patents in all countries that honor the WTO agreements remain in effect 20 years from the filing date. In the Pharmaceuticals industry, however, patents are filed as soon as a target is identified, so that by the time a drug gets to market, it may have only 10 or so years of protection left. Because the patent is granted when the new entity is discovered, every day spent in clinical testing and regulatory approval means one less day the drug will enjoy patent protection once it hits the market. To remedy this, innovative drugs may apply for patent extensions for up to five years after patent expiration. Additional safeguards are also put in place by mandating a period of data protection, which prohibits regulators from referring to clinical trial data generated by one drug company when they are evaluating another company's product.

Being first to market with a drug to treat a particular indication or disease could significantly benefit a drug company and establish that company as the clear market leader. Often, the first-to-market drug maintains a leading market share for many years. A first-to-market drug holds, on average, a 6% market share advantage 10 years after the drug launched, according to a study by McKinsey & Co. A big reason first-to-market drugs often achieve leading market share for so long is their exclusivity rights. Below is a list of the different types of exclusivity offered by the FDA.

- **Five-Year New Chemical Entity.** This exclusivity applies to a brand-name drug that contains a new chemical entity (NCE), which is a drug substance that contains an active ingredient or moiety(ies) never previously approved by the FDA. This exclusivity generally blocks the submission of any ANDA that contain the same active moiety for five years.

- **Three-Year New Clinical Studies**. This exclusivity attaches to a brand-name drug approved for a new use for a previously approved drug product. Applications for such new uses must be supported by information from new clinical investigations essential to approval of the new use, and conducted or sponsored by the applicant. Such new uses could include changes in strength, dosage form, route of administration, or indication.

- **Orphan Drug**. Certain drugs designated for the treatment of a rare disease or condition (*e.g.,* one affecting fewer than 200,000 people in the U.S. each year) are eligible for orphan-drug exclusivity upon approval. This exclusivity prevents approval of any other application (brand-name or generic) for the same drug for the same orphan-protected use during a seven-year period.

- **Pediatric**. This type of exclusivity is granted to a brand-name drug for which pediatric clinical studies have been conducted in response to a written request for such studies from the agency. Generally, pediatric exclusivity attaches to existing patents or exclusivities associated with the product line for the brand-name drug for six months.

- **GAIN**. The "Generating Antibiotic Incentives Now" (GAIN) exclusivity generally provides for an additional five years of exclusivity added to certain other exclusivity periods for a drug product that has been granted a "Qualified Infectious Disease Product" designation by the FDA.

- **180-Day**. This type of exclusivity may be granted to the first generic applicant(s) to submit a substantially complete ANDA that contains a challenge to a patent listed in the Orange Book, which is issued by the U.S. FDA (see Glossary). The generic drug applicant found to be eligible for this exclusivity has an exclusive right to market the generic drug for 180 days. Only ANDAs are eligible for this exclusivity.

After Patent Expiration Comes the Generic/Biosimilar Stage

Generic drug companies do not have the same high costs of R&D, tough regulatory approval, and sales and marketing as the companies developing new branded drugs, so generic drug companies can afford to discount their products. Generic drug manufacturers set prices depending on the kind of molecule they are making, how easy it is to manufacture, and, most importantly, how many generic competitors they expect to face.

When some easy-to-manufacture blockbuster drugs go off patent, half a dozen or more generic competitors may enter the market simultaneously at prices that are 80% or more below brand pricing. In less competitive situations, involving drugs that maintain some barrier to entry (such as special manufacturing skills or biological aspects) or those that have exclusivity for a limited time post-launch, fewer competitors come into the market at the same time, and pricing, at least initially, is more stable. As more competitors enter the field, prices drop even further.

Health Technology Assessment

Rapid advances in medical technology, which is expensive, necessitate that users are well informed about the cost-effectiveness of drugs, therapies, and medical devices. The Health Technology Assessment (HTA) analyzes cost-effectiveness and produces scientific comparative assessments of the benefits or detriments of medical outcomes for these variables, which are then used by national health care authorities to make pricing and reimbursement decisions. The HTA focuses on economic effectiveness for different technologies, whereas regulatory approval systems examine the safety and efficacy. The HTA, as a discipline, examines new, expensive technologies and pharmaceuticals thoroughly to gauge cost-effectiveness. However, patients are more concerned about reimbursement than costs.

Most countries use one form or another of the HTA to help bridge the gap between research cost and pricing decision-making. For example, in the U.K., the NICE, whose opinion is considered for the pricing and reimbursement decisions, evaluates the economic benefits of new technologies using HTA reports. Meanwhile, the EU, in order to enhance coordination at the EU level, adopted the Regulation on HTA in December 2021. In Japan, following a three-year pilot program, the Japanese government launched the cost-effectiveness assessment (CEA) in April 2019. CEA has been devised as a tool to supplement the current drug pricing system.

Regulatory Environment

U.S.

The FDA is responsible for regulatory oversight of the pharmaceuticals and medical technologies industries in the U.S. The Prescription Drug User Fee Act (PDUFA), a program initiated in 1992 that charges drug makers a fee for filing New Drug Applications (NDAs), has been credited with significantly reducing new drug approval times as the funds are used to hire new FDA personnel. Since its inception in 1997, PDUFA has allowed seriously ill patients easier access to experimental compounds and provided new incentives for the development of pediatric medicines. It also expanded drug companies' ability to disseminate information on off-label uses of new and existing drugs.

On August 18, 2017, the U.S. president signed the Food and Drug Administration Reauthorization Act, including the reauthorization of the PDUFA for fiscal year 2018 through fiscal year 2022. (The U.S. fiscal year runs from October 1 of one year to September 30 of the following year.) For fiscal year 2022, the FDA projected a base revenue amount of $969.8 million, representing a 16.7% increase from fiscal year 2019.

The U.S. does not have universal health care coverage. Most citizens are covered by a combination of private and public sources such as Medicare (federal health insurance program for people who are 65 or older, certain young people with disabilities, and people with End-Stage Renal Disease) and Medicaid.

U.K.

The Department of Health and Social Care (DHSC) formulates policies at the national level and issues directives to the National Health Services (NHS), which in turn manages health care in the U.K. The NHS introduced clinical commissioning groups (CCGs), which can commission any provider that meets NHS standards on price, quality, and safety.

Based on the NHS constitution, U.K. citizens have the right to drugs and treatments recommended by the National Institute for Health and Care Excellence (NICE), if determined clinically appropriate. NICE, which conducts risk-benefit analysis in order to help the government determine reimbursement rates and strategies, played an increasingly visible and controversial role in determining which drugs get reimbursed in the U.K.

Drug prices in the U.K. are subject to control through the voluntary scheme for branded medicines pricing and access (the Voluntary Scheme) or the Statutory Scheme established under the Branded Health Service Medicines Regulations 2018. The Voluntary Scheme is subject to renegotiation every five years. The current five-year scheme began on January 1, 2019 and will run until the end of 2023. The scheme limits pharmaceutical companies' return on capital and requires that excess profits be returned to the NHS, effectively capping profits and encouraging companies to set lower drug prices. On the other hand, pharmaceutical companies that choose not to join the Voluntary Scheme are automatically subject to the Statutory Scheme. However, the scope of the scheme only extends to prescription-only medicines.

Europe

The European Medicines Agency (EMA) is responsible for the scientific evaluation of centralized marketing authorization applications (MAA). Based on the recommendation of the EMA, the European Commission approves the marketing of drugs in the EU. Once granted by the European Commission, the centralized marketing authorization is valid in all EU Member States, Iceland, Norway, and Liechtenstein.

Despite the establishment of the EMA, differences still exist within EU Member States. Even after a drug is approved, the time it takes to enter the respective markets varies from country to country and is dependent on the time it takes for the respective regulatory authorities to negotiate reimbursement prices with pharmaceutical companies. As negotiated prices vary between states, price differentials exist

(sometimes within different regions of a state), giving rise to a parallel trade that involves importing medicines from another state where the drug is sold for less.

Below are examples of regulatory environments in major European countries.

- **Germany**

In Germany, there is universal coverage for legal residents — about 90% of the population is covered by statutory social health insurance (SHI) or GKV (gesetzliche Krankenversicherung), while the remainder is covered by substitutive private health insurance (PHI), according to GKV-Spitzenverband's website.

Over the past couple of decades, the German health care system has undergone several reforms. The first health care reform in 2007 required employers to pay a certain percentage of salary to the health fund, which would in turn disburse money to the respective insurance plans. The reform allowed SHI to determine the maximum reimbursement price for patented drugs based on the cost benefit assessment performed by the Institute for Quality and Efficiency (IQWiG), thereby increasing competition among insurance players and, subsequently, pharmaceutical companies.

Prior to 2016, employers and employees were required to share the health fund contribution rate of 14.6% of gross salary equally. Employees were also required to contribute an additional 0.9% plus supplementary per capita premiums set by sickness funds. The two requirements were subsequently abolished in 2016 and replaced with a supplementary income-dependent contribution rate determined individually at an average of 1.1%. Such contributions are centrally pooled and redistributed to individual sickness funds determined through a risk-adjusted capitalization formula.

In Germany, drug pricing is fixed, where retail prices for prescription drugs are determined by adding a margin of 3% to the wholesale price, plus a fixed pharmacy service compensation fee of €8.35 and the value-added tax.

- **France**

France's health care system is executed by both national and regional authorities, with the budget for health care expenditure approved by parliament. The Ministry of Health performs several functions, including allocation of funds to regions and setting prices for reimbursable drugs. At the regional level, there are hospital agencies that allocate funds to public hospitals. Since 2004, the Ministry of Health and statutory health insurers have shared responsibility for defining the benefit package, as well as setting price and cost-sharing levels in the health care system.

The French health care system covers nearly all its population and is financed via a combination of tax revenue and mandatory contributions from employers and employees based on percentage of income. Health care is provided by hospitals, which may be public or private. Benefits covered under the statutory insurance plan include access to outpatient care, diagnostic services, drugs, devices, and preventive care facilities. Patients are initially required to pay for services and later are reimbursed by the public insurance funds. Patients are required to make co-payments to cover expenses that are not covered by the statutory insurance plan. In practice, people purchase private insurance to cover these co-payment charges.

The Agence Nationale de Sécurité du Médicament et des produits de santé (ANSM) approves market authorization of new drugs for use in France as a formality with the EMA. The ANSM regulates medicine manufacturing, marketing, and other health product safety issues.

- **Italy**

Italy adopts a tax-funded universal health care system called the National Health Service (Servizio Sanitario Nazionale or SSN) that closely models the British system. Under this system, SSN coverage is automatic and universal for legal residents. Since coverage is mandatory, substitutive insurance does not exist; however, complementary and supplementary private health insurance are available.

The system is highly decentralized and has three levels. At the national level, the Ministry of Health formulates a health care plan (Piano Sanitario Nazionale or PSN) that determines health care policies every three years. At the regional level, the 19 regions and two autonomous provinces implement the PSN with their own resources and adjust according to region-specific needs. Hence, differences exist in terms of health care access or level of co-payment. At the local level, local health units (Azienda Sanitaria Locale, or ASLs) provide health care services, including primary medical services and coordination of all non-emergency admissions to public hospitals.

At the national level, the Italian Medicines Agency (AIFA) evaluates pricing and reimbursement dossiers with support from the Pricing and Reimbursement Committee (CPR) and the Technical Scientific Committee (CTS). At the regional level, a therapeutic commission decides on formulary inclusion/exclusion, while at the local level, ASLs distribute funding to hospitals through formularies, or hospital pharmacists purchase drugs based on formularies by regional health authorities.

General conditions of the reimbursement system are established at the national level and are implemented at the regional level by governmental bodies. If a manufacturer seeks reimbursement in Italy, the price for the product will be set through negotiations between the manufacturer and the CPR. Unlike the U.S., German, and French health care systems, there are no mandatory rebates in Italy, which implements a more transparent pricing system.

When marketing authorization is granted by either the EMA or the AIFA, the company may apply for reimbursement on the National Pharmaceutical Formulary (PFN). A product can be assigned to Class A (products for chronic diseases, fully reimbursed), Class H (fully reimbursed only in hospitals), or Class C (not reimbursed).

- **Spain**

The Spanish national health system, called the Sistema Nacional de Salud (SNS), offers universal coverage and a wide variety of services with a network of hospitals and primary-care centers. Spain does not allow users to opt-out; hence, 99% of Spain's population uses universal coverage supplemented by PHI for faster and higher-quality treatment. The Ministry of Health is Spain's government agency for coordination of national health issues, legislation on medicines, broader health issues, and international health relations and agreements. The Spanish health care system is highly decentralized and is administered by 17 autonomous communities. However, the degree and speed of decentralization vary across regions.

Spanish drug prices, which are among the lowest in Europe, have fallen due to continuing mandatory price cuts. Industry margins were squeezed as a result of the government's strategy to promote the use of generics, impose reference prices on off-patent drugs, and limit price premiums to innovative drugs. Under the SNS, reimbursement rates are divided into three categories: 100% for hospital care medicines; 90% for management of chronic diseases (*e.g.,* diabetes, asthma, and epilepsy); and 60% for most prescription-only medicines. The pricing of a drug is determined upon reimbursement approval. If reimbursement is not approved, pharmaceutical companies are free to set prices as sale of non-reimbursable drugs are limited unless they are innovative, novel treatments.

Prices of drugs approved for reimbursements are set based on a mandatory price application document, which includes cost per day compared with equivalent products in Spain, the price of the product in other EU countries, a sales forecast, and the overall cost of R&D and production costs. Spain's constitution provides freedom to all regions to set their own price caps or cost-containment targets for drugs approved for reimbursements.

- **Switzerland**

Switzerland's Federal Health Insurance Act of 1994 regulates the health care system and made health insurance compulsory for all Swiss residents. Switzerland has one of the most market-oriented universal health care systems, with the idea of managed competition that leaves health insurance in private hands,

while creating a highly regulated market as a framework. Compulsory insurance (or basic package) is supplemented by private insurance providers and does not include dental care or access to higher-quality services.

Switzerland traditionally follows a decentralized structure where the 26 cantons or regions have a high degree of autonomy. With less government control, the Swiss health care system has been able to reduce waiting time for treatment and to encourage new technology and medicines. The federal government has taken specific measures to rein in health care costs through generic substitution, which has been in progress since 2001.

In Switzerland, the cost of drugs is generally higher than in other countries with similar economies, according to the OECD. In September 2018, the federal government set the maximum allowable public price for drugs in a move to reduce rising drug costs in the country. Drug prices depend on several factors such as their therapeutic value, availability of alternative treatments, and comparative prices of the same class of medicines in other European countries. Authorities and manufacturers negotiate maximum prices of drugs reimbursable by basic health insurance.

The Federal Office of Public Health (FOPH) regulates both inclusion on the positive list and the pricing of drugs reimbursed by the basic package. It sets maximum prices across the board, including those for branded drugs, off-patent drugs, and generics. The FOPH also regulates manufacturer prices as well as distribution margins and payments for services by pharmacists. Lastly, the FOPH also reevaluates pricing and reimbursement of drugs every three years to reduce the drug prices, according to Interpharma.

China

The National Medical Products Administration (NMPA), formerly the China Food and Drug Administration (CFDA), is the Chinese agency for regulating drugs and medical devices. The agency was initially founded in 1998 and was renamed on September 1, 2018. The NMPA is not only responsible for medical devices, but also for medicinal products, biological products, food, and cosmetics. The restructuring of the CFDA represents China's approach to upgrading its clinical research regulations. This is also aimed to improve the quality of health care available to the nationwide Chinese citizens and try to facilitate easier engagement with foreign companies to encourage investment and joint ventures. The National Health Commission is responsible for the overall guidance of health care reforms, administering China's Essential Drug List (EDL), as well as managing the drug procurement policies.

China's health insurance is publicly provided and mostly financed by the government. Its health insurance system has been gradually expanded to provide basic coverage for nearly 95% of the population. China's public health insurance can be broken down into three sub-categories: 1) basic coverage for urban enterprise employees, 2) basic coverage for other urban residents, and 3) rural cooperative medical insurance for the farming population.

To combat rising drug prices, public hospitals are required by mandate to impose a "zero mark-up" policy on drug sales. Under the previous practice, public hospitals were allowed to mark-up drugs by around 15% above procurement prices. With the new drug pricing policy, the drug prices that public hospitals charge to the patients would be the same as those paid to the drug suppliers.

On December 26, 2016, China launched a "two-invoice" system for drug distribution. The new system aimed to streamline the pharmaceutical procurement process, where the manufacturers of pharmaceutical products would directly perform delivery or commission a qualified distributor with modern logistics capacity to deliver the pharmaceutical products, followed by distributors to the end consumer (*e.g.,* hospital), eliminating multi-tiered distribution.

China launched its centralized procurement program as a pilot in 2018 and has since gone nationwide. The program is to control drug prices and improve patient accessibility to high-quality medicines. Under

the system, public hospitals are supplied with medicines purchased by a special working group through a bidding system. The working group decides beforehand the quantities of drugs to be procured to create lower prices and specifies the quantity on the bidding announcement. China's fifth batch of the centralized drug procurement concluded in June 2021, which saw an average price cut of 56% across 61 drugs.

Volume-Based Procurement (VBP) is the national tendering for off-patent drugs in China. VBP was first introduced in 2018, which kicked off national tendering on off-patent drug in China. There have been five rounds national-wide, while this mechanism would become normalized and institutionalized. Led by the National Healthcare Security Administration (NHSA), VBP bid winners will have sales guarantee for the committed volume (~70% of total hospital market) at the negotiated price with a two-year contract, while the remaining non-committed market (~30% of total hospital market) is still free-selection based. Off-patent drugs with more or equal to two generics that are approved in China and passed Generics Quality Equivalence Test (GCQE) are exposed to VBP risk. There are six rounds of national-wide VBP organized by NHSA with direct impact on off-patent originators since 2019 with average price cut level of >50%, with the highest at 99%. Over 200 molecules are involved, contributing beyond 20% of China's total market. VBP price cut levels vary across molecules because of competitiveness and cost of goods sold. Chemical drugs face strong price cut, while competition is milder in biologics – *i.e.*, all insulins won the bidding with an average price cut at 41%. The VBP mechanisms are: (1) VBP bidding rules – originator and GQCE Gx in same competition group; lowest tender price will be set as bid ceiling price; lowest price to win the bid. (2) Impact on winners – multiple winners to ensure national supply and share the 70% committed market volume by splitting provinces. (3) Impact on non-winners – the remaining 30% non-committed market is still free-selection; around 30% price cut enforced on originators after VBP becomes effective. VBP is regarded as China's version of patent cliff, as the originator will still experience enforced price cut (~30%) even on lost bid. Early planning on patent and launch strategy in China is crucial to prolong the product lifecycle.

Japan

Japan's Ministry of Health, Labour, and Welfare (MHLW) is responsible for medical care, pensions, labor, and childcare of Japanese citizens. The MHLW is also in charge of pharmaceutical regulatory affairs in Japan. The Pharmaceuticals and Medical Devices Agency (PMDA) was established in April 2004 to handle a wide range of activities from clinical studies to approval reviews, post-marketing review, and ensuring the efficacy and safety of clinical trials.

Japan adopts a national health insurance system called the "Universal Health Insurance Coverage System." Under this insurance system, all citizens are covered by public medical insurance. The Japanese health insurance market is the second-largest in Asia and the third-largest in the world. The most crucial issue the Japanese currently face is the rising cost of medical expenditures due to the increasing population of elderly people. Under the insurance system, the citizens will be able to obtain high-quality medical services at a low cost.

HOW TO ANALYZE A COMPANY IN THIS INDUSTRY

In evaluating a company in the Pharmaceuticals industry, the most important factors to consider are the company's products, markets, and financial health.

Researching the Business

A thorough examination of the company's products and markets is the first step in the analysis. A pharmaceutical firm's approved drug portfolio is the main ingredient of near-term success, while its development pipeline will determine its long-term prospects. Once the drugs are approved, the company needs to effectively get the drugs to market, too. A few important questions regarding a drug company's product portfolio and strategy are shown below:

Product Portfolio and Pipeline

◆ **Are sales comprised of prescription or non-prescription products?** Prices and profit margins of prescription drugs are significantly higher than non-prescription or over-the-counter (OTC) drugs. Non-prescription drugs are essentially mass-marketed consumer products. Patent protection is an important consideration for prescription drugs, whereas success of non-prescription drugs is more closely linked to brand-name recognition and promotional spending levels, in our view.

◆ **What therapeutic areas does the company focus on?** Most major prescription drug makers tend to focus on a few specific therapeutic markets. An important part of the analysis is understanding the competing companies and drugs in these different therapeutic areas, as well as the patient populations that are captured by them. This can help assess the riskiness and growth prospects for the respective drug maker.

◆ **When do the patents on the company's most important drugs expire?** If the expiration dates are within the next few years, is the company adequately preparing to make up for the revenues lost to generic competition? If a company loses its marketing exclusivity on key drugs without earning adequate profits from new products, it can find itself in difficult economic straits. Many of the leading drug makers are currently contending with fierce generics competition and ongoing patent expiration.

◆ **Have R&D efforts been productive?** In terms of R&D, the larger, well-funded firms typically have the advantage of being able to hire top scientists and to conduct more clinical trials, which are necessary to develop new drugs. Most leading drug makers spend between 14% and 18% of their revenues on R&D. However, their success rates – in terms of lucrative new drugs – differ markedly. In addition, R&D productivity can be cyclical.

Overall, companies with new drugs for novel treatment hold the keys to success. New products that provide essentially similar results as existing drugs are less likely to gain commercial success. For those companies that do not see their drug portfolios being reinvented, management often looks for cost savings through substantial M&A activities, and diversification of the product base with the intent of capturing growth opportunities in emerging markets.

Determined by the market opportunity and sales prospects – including levels of unmet medical need, competitiveness, and scientific challenge – R&D activity in disease areas such as hypertension and peptic ulcers has become less desirable, while R&D activity in oncology continues to show strong growth.

Company Attributes and Strategies

◆ **How large is the company?** For prescription and non-prescription drug makers alike, company size and market share are important considerations. Pharmaceutical firms must have the critical mass to support R&D, as new product development is crucial to future success. In addition, these companies

need to maintain a large sales force to market drugs in key domestic and foreign markets. Smaller drug companies, and even larger ones that depend heavily on one or two products, are more vulnerable to eventual patent expirations and competition from rival drugs.

With respect to market share, does the company dominate any key market? Key markets are typically those with a large population, whose chronic condition requires a daily regimen of maintenance therapy, thus offering the greatest sales opportunity. Medications for high blood pressure, elevated cholesterol levels, depression, ulcers, diabetes, and arthritis are examples. Oncology, once a niche therapeutic segment, is now exceedingly desirable given technological advances, growth rates, and profitability.

◆ **What is the company's acquisition strategy?** If a prescription drug maker is diversified or acquisitive, is this a plus or a minus? In our view, M&A activities including divestitures should be carefully analyzed to determine whether initial objectives such as strategic fit and synergies are being met and/or whether they are accretive or dilutive in terms of earnings, notably earnings per share (EPS) and operating margin. In general, large pharmaceutical companies regularly tap into smaller, more entrepreneurial companies as sources of innovation. Business development – the process of scouting for attractive deals and negotiating terms – is an integral part of a company's operating expertise and core strategy.

◆ **Has the company formed any promising alliances?** Large firms often benefit from alliances with smaller biotechnology and biopharmaceutical firms working on potentially lucrative new drugs. Conversely, a smaller company may find it necessary to team up with a larger partner to fund the clinical trials and commercialization of its discoveries.

Many companies also maintain relationships with scientists at leading medical colleges or other organizations, such as the U.S. government's National Institutes of Health, which can funnel experimental products to drug makers.

Business ventures with foreign companies can be a source of new products. For example, many drugs popular in the U.S. today were discovered by European and Japanese firms, but they are marketed by U.S. drug makers under royalty arrangements.

◆ **What is the company's international business profile?** The U.S. remains the most important market for U.S. drug makers, as well as for many international drug companies, because of its size and lack of government-imposed price constraints. That said, there have been continuous discussions on the effort to lower the drug price in the U.S. as both political parties aim for more affordable drug prices for Americans, although no major pricing reform have been implemented to date. Nonetheless, pharmaceutical markets elsewhere represent an attractive source of growth. Indeed, pharmaceutical sales in developing nations are expanding much faster than are those in the U.S.

◆ **How effective is the company in working with regulators?** Because all drugs sold in the major markets must first be cleared by the health care authorities like the FDA and the EMA, a firm must be able to work with these agencies and understand their criteria. Here again, size and experience can help. Most large, well-established drug companies are adept at working with the agencies, while many smaller or newer firms are less proficient and often encounter major snags in obtaining approval for their products.

◆ **How effective is the company at working with third-party government and private payers?** Reimbursement is crucial for the commercial success of a product. Private and public payers are taking an increasingly hard line in evaluating the cost-effectiveness of recently approved drugs. In Europe and Asia, several governments have established organizations to make recommendations on whether a new drug should be reimbursed – and in some controversial cases, they have argued against coverage. The U.S. has not taken this approach, although it is considering the establishment of a reimbursement evaluation organization. U.S. payers increasingly differentiate drugs within the same therapeutic class and placing them in separate tiers, with varying contributions from patients, aimed at incentivizing patients

to use certain drugs. The ability to negotiate fair deals over reimbursement for prescription drugs is also likely to be increasingly important to drug companies.

Nonprescription Drug Makers

While the prescription drug market depends on research-intensive innovation to differentiate among products and bolster sales, the nonprescription, or OTC, segment depends much more on consumer-directed marketing. The main factors that must be considered in evaluating an OTC drug company include the relative strength of its product offerings, its ability to develop new products, competitive pressures in each market segment, and the manufacturer's ability to support product sales through effective advertising and promotional campaigns.

Analyzing Financial Statements

When looking at a pharmaceutical company's financial statements, it is important to examine income statement trends such as sales growth, profit margins, R&D, and selling, general, and administrative (SG&A) expenses, as well as balance sheet items such as asset and debt levels. Equally important is evaluating how income statement items interact with the balance sheet in metrics such as return on invested capital.

◆ **Sales trends**. Examine the company's recent and historical sales performance. Has sales growth been consistent or volatile? How has growth been achieved: through volume, pricing, acquisitions, or through a combination of these?

Watch Out! *Pharmaceutical companies provide certain discounts and rebates to customers. They also allow returns and negotiate different prices with different final consumers of the product. Therefore, management must make a variety of estimates in calculating provisions for appropriate allowances at the time of sale. These provisions (and the corresponding level of allowances) have a direct impact on reported revenues. Because these are management's estimates, we caution that in robust periods management may provision very high levels and in leaner times may use these excess reserves to boost sales and income.*

◆ **Operating margins.** Higher operating margins can reflect valuable competitive advantages that a drug maker may possess, such as premium pricing on high-demand drugs with limited competition, efficient production facilities, or low raw material costs. SG&A expense margins that are lower than industry-average are also an indication of a well-managed company.

Watch Out! *It is common for pharmaceutical companies to monetize certain intangible assets by selling the rights to a product to another entity. In instances where these sales are recognized as revenue, gross margins are likely boosted due to the lack of related cost of goods sold. Additionally, CFRA raises concern related to the one-time nature of such revenues and believes that these sales essentially pull forward all revenues related to that asset into one reporting period.*

◆ **R&D expenses.** R&D is an important aspect of pharmaceutical operations for ensuring long-term sustainability, particularly to replace successful drugs once they lose exclusivity. The R&D expense margin should be monitored to ensure a company isn't cutting R&D to boost short-term profits. The whole dollar amount of R&D should be evaluated as well, as a drop in sales can mask a large cut in the R&D budget that wouldn't be revealed by a large drop in R&D margin.

◆ **Pre-tax earnings.** While operating earnings reflect a company's performance in making and selling its products, it doesn't capture the cost of debt capital that may have been used to acquire some of the operating assets. It is important to measure a firm's earnings growth through pre-tax earnings, as well as operating earnings, to assess the impact that interest expense has on net profits.

Watch Out! *Pharmaceutical companies can have high insurance costs related to product liability, workers' compensation, and health care benefit costs, and some portion of these insurance costs may be self-insured. Companies that provide self-insurance are required to estimate and accrue costs related to the above noted items. To the extent that these accruals are subject to management discretion, they may be manipulated to achieve a financial performance target. We would normally expect accruals related to workers' compensation and employee health benefits to grow or decline at a rate similar to that of the business. Any deviation could be a sign of earnings management.*

◆ **Adjusted EPS.** Among the most important financial metrics for investors in the Pharmaceuticals industry, EPS performance is widely monitored because it combines several important factors, including a company's ability to increase revenues, control operating expenses, and manage capitalization, as interest expense on debt and equity share count also factor into EPS. "Adjusted" refers to management's discretionary removal of certain non-operating items from the earnings calculation. These often include one-time legal expenses or non-cash amortization expenses resulting from acquisitions.

Watch Out! *Significant and/or recurring use of special charges is a red flag that a company may be using these charges to flatter non-GAAP results. We caution that companies may boost non-GAAP earnings in the current period by bundling normal, recurring costs into the special charges.*

◆ **Return on invested capital.** In measuring the long-term performance of a company, pre-tax return on invested capital/ROIC [EBIT/(debt + equity)] is a good metric to use in addition to long-term EPS growth, as it analyzes how much capital management required to produce the earnings growth. If invested capital is growing faster than earnings for a prolonged period, it may be the case that management is not putting incremental capital to its highest and best use, and this would be indicated by declining ROIC.

◆ **Cash Flow Statement.** Another useful analysis involves looking at operating cash flow (essentially, net earnings plus depreciation and other noncash charges) and investing activities on the Cash Flow Statement. This provides a useful gauge of a company's ability to generate true cash earnings and its capacity to finance capital projects. Firms investing heavily in acquisitions and capital projects are preparing to expand the business. Those paying out more in dividends and share repurchases may have fewer opportunities for future growth.

Using the Balance Sheet to Assess Financial Health

The balance sheet is a snapshot of a company's financial condition at a specific moment in time, so it should be examined to determine a company's financial health.

◆ **Operating Assets.** Generating sales requires maintaining invested capital in several large asset accounts. This capital takes the form of either debt or equity and is used to fund such items as accounts receivables, inventories, manufacturing plants, R&D facilities, and office buildings. These accounts tend to grow as companies expand, requiring greater capital investment.

Watch Out! *R&D costs should be expensed as incurred until the related product has reached commercial feasibility, which, in this industry, normally occurs when a product is approved by the FDA. A material increase in capitalized R&D costs not explained by the timing of FDA approval may indicate over capitalization of R&D, which could pressure future earnings growth.*

◆ **Cash.** Investors look at a company's level of cash and marketable securities to assess short-term liquidity. The proper level of cash and cash equivalents varies from company to company. Subtracting outstanding debt from cash balances provides a more stringent measure of a company's actual financial strength.

◆ **Current ratio.** Another reliable measure of liquidity is the ratio of current assets to current liabilities. The current ratio measures a company's ability to pay its bills. A higher-than-average current ratio

indicates financial strength, since current assets are readily available to be converted into cash. Any meaningful degradation in the current ratio from previous reporting periods may signal a liquidity problem.

◆ **Long-term debt-to-capital ratio.** This ratio is calculated by dividing long-term debt by total capital (the sum of long-term debt and stockholders' equity). A relatively low percentage indicates that the company may be less burdened than its peers in terms of debt service. An appropriate debt load depends largely on a company's product lines and projected new product streams. Any sudden change in the company's attitude toward taking on debt should be thoroughly investigated.

Valuation Measures

Investors typically use various valuation metrics to help them determine a stock's value and compare it to the current price. Common measurements usually include multiples of key income statement entries such as sales, earnings, and earnings before interest, tax, depreciation, and amortization (EBITDA), often in ratios combined with past or future growth rates. Valuations can also encompass a number of balance sheet metrics, such as return on assets (ROA), return on equity (ROE), and return on invested capital (ROIC). With any valuation metric, the challenge is often forecasting future operating performance.

◆ **P/E Ratio.** The price-to-earnings (P/E) ratio is widely used to compare a company's valuation against peers. Of particular interest to most investors is the P/E ratio using a next-twelve-months estimate of EPS for the denominator. This metric tells an investor how much they are paying today for each dollar of earnings expected to be delivered to shareholders in the next year. If a company's earnings are expected to grow rapidly over the next several years, investors are usually willing to pay a higher P/E, and vice versa, as they expect the high price today will be justified by higher earnings down the road.

◆ **PEG Ratio.** Taking the P/E metric a step further, dividing the P/E ratio by a company's expected long-term earnings per share (EPS) growth rate yields a P/E-to-earnings growth (PEG) ratio. The PEG puts the P/E ratio in the context of a company's longer-term growth prospects rather than just on the basis of one year of earnings. A company that looks very expensive on a P/E basis may actually be reasonably priced on a PEG basis after considering its excellent long-term growth prospects. A higher growth rate will bring the PEG ratio down, relative to a slower EPS growth rate.

◆ **Discounted Cash Flow (DCF) Analysis.** Another key valuation metric applied widely with pharmaceutical stocks is a DCF analysis. This tool projects a company's future cash flows out several years, then discounts the amounts by an investor-specific cost of capital to arrive at a per share present value for the firm. If the calculated per share DCF value is higher than the current stock price, the stock may be an undervalued investment opportunity.

GLOSSARY

180-day exclusivity—The first generics company to file a completed Abbreviated New Drug Application (ANDA) challenging the patent of a brand-name drug gets 180 days of exclusivity; only that company can market the generic for six months following the expiration of the branded drug's patent. Two generics companies can share exclusivity if they filed patent challenges for different doses. The maker of the brand-name drug also has the right to market an "authorized generic" following patent expiration.

Abbreviated New Drug Application (ANDA)—The application filed for approval of generic drugs by the U.S. Food and Drug Administration (FDA). ANDAs require substantially less information than new drug applications (NDAs) for prescription drugs, because applicants have to prove only that their products are identical (bioequivalent) to the brand products. (See *Bioequivalence*.)

Active moieties—In organic chemistry, a moiety is part of a molecule or ion. Active moieties are the smaller chemical pharmacophoric elements or three-dimensional structure that are responsible for the physiological or pharmacological action of the drug substance.

Adeno—Prefix referring to a gland, as in adenoma and adenopathy.

Authorized generic—A generic version of a branded drug, made by the manufacturer or by a company that has been approved by the manufacturer. It is identical to the branded drug but has a different label. Innovator manufacturers use authorized generics to take some of the profits that are gained by generics companies from 180-day exclusivities.

Bioequivalence—Drugs that have the same rate and extent of absorption into the body when administered at the same dose and under similar conditions are described as bioequivalent. Such products can be substituted for each other without a dosage adjustment to obtain the same therapeutic effect.

Biogenerics—Also known as follow-on proteins and biosimilars, biogenerics are copies of therapeutic proteins launched after patent expiry of the main active ingredient. Like traditional generics, they must have the same qualitative and quantitative composition, active substances, and pharmaceutical forms as the innovative product. Unlike traditional generics, they may be 'biosimilar' instead of identical and are likely to require independent proof of efficacy and safety.

Biological—A medicine (*e.g.*, vaccine, antigen, serum, or plasma) made of large protein molecules that are derived from living organisms or their byproducts, not from chemicals; also called a biologic.

Biotechnology—Any technological application that uses biological systems, living organisms, or derivatives to make or modify products and processes. The approach differs from traditional drug development, which relies on synthetic chemistry and results in small-molecule, easy-to-administer treatments that come in pills and tablets. Biotech products consist of larger molecules that are harder for the body to absorb and thus often have special administration requirements, such as injections.

Clinical trials—Tests through which experimental drugs are administered to humans to determine their safety and efficacy. Trials occur in three phases. Phase I tests for safety. Phase II concerns efficacy. Phase III involves tests on larger numbers of subjects, usually several hundred to several thousand people. Phase III trials are usually randomized and double blinded and often last several years. Successful completion of Phase III allows a company to file with regulatory agencies for marketing approval.

Exclusivity period—A 180-day period during which a generics company has the right to be the exclusive seller of a generic for six months following the end of patent protection if that generic company was the first to file an approval application for the drug with the FDA, and simultaneously challenged the drug's then seemingly valid patent.

Formulary—A continually updated list of prescription drugs approved for reimbursement by a private insurer or government-sponsored health care program.

Gene—The basic determinant of heredity, genes are chromosomal segments that direct the syntheses of proteins and conduct other molecular regulatory functions.

Generic drug—A compound that contains the same active ingredients as a branded drug. A company cannot market a generic version of a rival's branded product until its patent expires.

Genomics—The study of genes and their functions, including mapping genes within the genome, identifying their nucleic acid structures, and investigating their functions.

Good Manufacturing Practice (GMP)—A code of standards concerning the manufacture, processing, packing, release, and holding of a medicine.

GM1 gangliosidosis—An inherited disorder that progressively destroys nerve cells (neurons) in the brain and spinal cord.

Investigational new drug (IND)—An experimental new compound that has successfully completed animal studies and has been approved by the FDA to proceed to human trials.

Managed care—A supervised system of financing and providing health care services for a defined population group.

Medicare Part B—A medical insurance coverage that helps to pay for services from doctors and other health care providers, outpatient care, home health care, durable medical equipment, and some preventive services.

Medicare Part D—A Medicare prescription drug coverage that helps to cover the cost of prescription drugs.

New drug application (NDA)—The formal filing that drug makers submit to the FDA for approval to market new drugs. The document must contain clinical evidence of the compound's safety and efficacy.

New molecular entity (NME)—A new chemical entity (NCE) or biological product, intended for use in a prescription medicine, that has not received government approval for use in humans.

Novel drugs—Drugs that are categorized by the U.S. FDA's Center for Drug Evaluation and Research (CDER) as innovative medicines that help advance clinical care to another level.

Orange Book—The publication Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book) identifies drug products approved on the basis of safety and effectiveness by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (the Act) and related patent and exclusivity information.

Orphan drug—A drug designed to treat rare diseases afflicting a relatively small patient population. The U.S. government gives drug makers special incentives to encourage the development of such drugs.

Over-the-counter (OTC) drugs—Compounds sold in pharmacies and other outlets without need of a prescription; also known as proprietary medications.

Prescription Drug User Fee Act (PDUFA)—An Act created by Congress in 1992 that authorizes FDA to collect user fees from persons that submit certain human drug applications for review or that are named in approved applications as the sponsor of certain prescription drug products.

Prior authorization—A requirement that a physician obtain approval from the patient's health insurer before prescribing a specific medication.

Therapeutic substitution—A policy that some managed care organizations employ to substitute less expensive drugs for more expensive ones in the same therapeutic class, although drugs use different modes of action.

Treatment IND—An FDA program that allows experimental drugs (INDs) that treat life-threatening diseases to be made commercially available to very sick patients before the drugs obtain formal FDA approval.

INDUSTRY REFERENCES

PERIODICALS

DCAT Value Chain Insights
www.dcatvci.org
An online information resource offering news and analysis on the issues impacting the business of pharmaceutical development.

Fierce Pharma
fiercepharma.com
Delivers breaking news and analysis about drug companies, the FDA, and the broader pharma industry.

Financial Times
ft.com
One of the world's leading news organizations, recognized internationally for its authority, integrity, and accuracy.

Generics and Biosimilars Initiative
gabionline.net
An authoritative resource for global news on recent developments in the field of generics and biosimilars, a repository of worldwide guidelines, and an archive of related scientific information.

Pharma Manufacturing
pharmamanufacturing.com
A site for news, and analysis on pharma and biopharma manufacturing and operations.

Pharmaceutical Technology
pharmaceutical-technology.com
A site focusing on the latest news on pharmaceutical markets from biotechnology to therapeutics, vaccines, and more.

Pink Sheet
pink.pharmamedtechbi.com
An online newsletter that covers trade in, and regulation of, pharmaceuticals and biotechnology.

Reuters
reuters.com
An international news organization, covering breaking news in markets, politics, and technology.

The American Journal of Managed Care
ajmc.com
An independent, peer-reviewed medical journal dedicated to disseminating clinical information to managed care physicians, clinical decision makers, and other health care professionals.

The New York Times
nytimes.com
An American news organization based in New York City with worldwide influence and readership.

BOOKS

Merck Manuals
merckmanuals.com
Provides detailed information for physicians on various diseases and medical conditions, and on therapeutics for treating them.

Physicians' Desk Reference
pdr.net
An annual compendium listing commercial prescription drugs and their FDA-approved prescribing information.

TRADE ASSOCIATIONS

American Cancer Society
cancer.org
A nationwide voluntary health organization dedicated to eliminating cancer.

American Pet Products Association
americanpetproducts.org
A leading trade association serving the interests of the pet products industry; provides market research on the pet product industry.

Association for Accessible Medicines
accessiblemeds.org
A trade association representing manufacturers and distributors of generic drugs in legislative, regulatory, and related matters.

Association of the British Pharmaceutical Industry
abpi.org.uk
A trade association representing 120 prescription drug makers from the U.K. that invest in the discovery of new medicines for the future.

Biotechnology Innovation Organization
bio.org
A trade association representing the world's leading biotechnology companies in business, legislative, and regulatory affairs.

Consumer Healthcare Products Association
chpa.org
A trade association representing manufacturers and distributors of OTC medicines and dietary supplements; promotes industry interests in legislative and regulatory arenas; and publishes information on the OTC drug industry.

European Federation of Pharmaceutical Industries and Associations
efpia.eu
A coalition of national pharmaceutical organizations of a number of European countries, along with various major pharmaceutical companies from all over the world.

Pharmaceutical Care Management Association
pcmanet.org
A national association representing America's pharmacy benefit managers (PBMs), which administer prescription drug plans for more than 266 million Americans.

Pharmaceutical Research and Manufacturers of America
phrma.org
A trade association representing the country's leading research-based pharmaceutical and biotechnology companies in legislative and regulatory affairs.

RESEARCH FIRMS

Center for Security and Emerging Technology
cset.georgetown.edu
A policy research organization within Georgetown University that produces data-driven research at the intersection of security and technology.

Decision Resources Group
decisionresourcesgroup.com
A market research and publishing firm focusing on the pharmaceuticals and biotechnology industries.

Deloitte
deloitte.com
A research firm that provides audit, consulting, financial advisory, risk advisory, tax, and related services.

EvaluatePharma
evaluate.com
Provides consensus forecasts from leading industry analysts, and analysis of the health care sector.

Fitch Solutions (Previously BMI Research)
fitchsolutions.com
Provides macroeconomic, industry, and market analysis.

IQVIA
iqvia.com
A market research firm specializing in pharmaceuticals.

National Institute for Health Care Management Foundation
nihcm.org
A non-profit, nonpartisan group that conducts research on health care issues.

The Henry J. Kaiser Family Foundation
kff.org
A private non-profit foundation focused on U.S. health care issues; publishes studies on a variety of health care topics.

GOVERNMENT AGENCIES

Centers for Medicare & Medicaid Services
cms.gov
A division of the U.S. Department of Health and Human Services; administers Medicare and Medicaid programs and sets rates at which program providers are compensated.

Department of Justice
justice.gov
A **federal executive department of the** U.S. **government tasked with the enforcement of federal law and administration of justice**.

European Medicines Agency
ema.europa.eu
A pharmaceutical regulatory body for the EU; oversees marketing approvals for the EU.

Germany Invest & Trade
gtai.edu
An economic development agency of the Federal Republic of Germany.

Ministry of Health, Labour and Welfare of Japan
mhlw.go.jp
A cabinet level ministry of the Japanese government that provides regulations concerning food and drugs.

National Center for Health Statistics
cdc.gov
A division of the Centers for Disease Control and Prevention; provides U.S. data on diseases, pregnancies, births, mortality, and other categories.

National Institutes of Health
nih.gov
A government agency that provides major R&D funding in the life sciences in the U.S.

National Medical Product Administration
nmpa.gov.cn
A Chinese agency that regulates drugs and medical devices; responsible for drafting laws and regulations for drugs, medical devices, and cosmetics.

Organisation for Economic Co-operation and Development
oecd.org
An international forum with 30 member countries that seeks to foster economic development and free trade.

Pharmaceuticals and Medical Devices Agency
pmda.go.jp
A Japanese agency for ensuring safety, efficacy, and quality of pharmaceuticals and medical devices in Japan.

U.S. Food and Drug Administration
fda.gov
U.S. government agency charged with overseeing the food and pharmaceuticals industries; controls and supervises the approval and sale of new drugs.

World Health Organization
who.int
Directs international health initiatives within the United Nations' system and leads partners in global health responses.

World Trade Organization
wto.org
A global trade organization that regulates international trade between members by resolving disputes and establishing rules for such issues as intellectual property protection and fair competition.

ONLINE RESOURCES

Biotechgate
biotechgate.com
A global business development database containing over 50,000 company profiles and providing information on available biotech and pharma assets, financing rounds, key management, technology platforms, and more.

Our World in Data
ourworldindata.org
A non-profit organization based in the U.K. providing scientific online publication that focuses on global problems.

COMPARATIVE COMPANY ANALYSIS

					Operating Revenues															
					Million $							CAGR (%)			Index Basis (2012=100)					
Ticker	Company	Country		Yr. End	2021	2020	2019	2018	2017	2016	2015	10-Yr.	5-Yr.	1-Yr.	2021	2020	2019	2018	2017	2016
PHARMACEUTICALS																				
4503	ASTELLAS PHARMA INC.	Japan	#	MAR	0.0	11,297.8	12,089.4	11,789.1	12,243.5	11,763.8	12,217.0	2.7	-1.9	-3.9	0	92	99	96	100	96
AZN	ASTRAZENECA PLC	United Kingdom		DEC	37,417.0	26,617.0	24,384.0	22,090.0	22,465.0	23,002.0	24,708.0	1.1	10.2	40.6	151	108	99	89	91	93
BHC	BAUSCH HEALTH COMPANIES INC.	Canada		DEC	8,434.0	8,027.0	8,601.0	8,380.0	8,724.0	9,674.0	10,442.0	13.3	-2.7	5.1	81	77	82	80	84	93
BAYN	BAYER AKTIENGESELLSCHAFT	Germany		DEC	50,131.9	50,642.2	48,866.6	42,067.8	42,044.9	36,886.9	50,051.6	1.9	4.8	6.5	100	101	98	84	84	74
BMY	BRISTOL-MYERS SQUIBB COMPANY	United States		DEC	46,385.0	42,518.0	26,145.0	22,561.0	20,776.0	19,427.0	16,560.0	8.1	19.0	9.1	280	257	158	136	125	117
WEED	CANOPY GROWTH CORPORATION	Canada	#	MAR	0.0	434.6	281.3	169.3	60.4	29.9	9.8	NA	112.2	37.1	0	4438	2873	1729	617	306
CTLT	CATALENT, INC.	United States		JUN	3,998.0	3,094.0	2,518.0	2,463.4	2,075.4	1,848.1	1,830.8	10.1	16.7	29.2	218	169	138	135	113	101
4519	CHUGAI PHARMACEUTICAL CO., LTD.	Japan		DEC	8,681.8	7,624.9	6,314.0	5,284.5	4,742.7	4,212.2	4,150.1	10.3	15.2	27.0	209	184	152	127	114	101
4568	DAIICHI SANKYO COMPANY, LIMITED	Japan	#	MAR	0.0	8,702.8	9,124.3	8,390.2	9,041.0	8,566.1	8,779.3	-0.1	-0.5	-2.0	0	99	104	96	103	98
4523	EISAI CO., LTD.	Japan	#	MAR	0.0	5,840.4	6,464.8	5,801.2	5,650.0	4,835.0	4,876.5	-1.7	3.3	-7.1	0	120	133	119	116	99
LLY	ELI LILLY AND COMPANY	United States		DEC	28,318.4	24,539.8	22,319.5	21,493.3	19,973.8	21,222.1	19,958.7	1.5	5.9	15.4	142	123	112	108	100	106
GSK	GLAXOSMITHKLINE PLC	United Kingdom		DEC	46,192.4	46,555.3	44,704.3	39,281.9	40,800.2	34,434.3	35,279.5	2.2	4.1	0.0	131	132	127	111	116	98
JNJ	JOHNSON & JOHNSON	United States	#	JAN	0.0	93,775.0	82,059.0	81,581.0	76,450.0	76,450.0	71,890.0	3.7	5.5	13.6	0	130	114	113	106	106
MRK	MERCK & CO., INC.	United States		DEC	48,704.0	41,518.0	39,121.0	42,294.0	40,122.0	39,807.0	39,498.0	0.1	4.1	17.3	123	105	99	107	102	101
MRK	MERCK KOMMANDITGESELLSCHAFT A	Germany		DEC	22,389.4	21,448.3	18,125.9	16,986.5	17,431.6	15,859.8	13,950.6	6.7	5.6	12.3	160	154	130	122	125	114
VTRS	VIATRIS INC.	United States		DEC	17,886.3	11,946.0	11,500.5	11,433.9	11,907.7	11,076.9	9,429.3	11.3	10.1	49.7	190	127	122	121	126	117
NOVN	NOVARTIS AG	Switzerland		DEC	52,877.0	49,898.0	48,677.0	46,099.0	43,404.0	49,386.0	50,387.0	-1.2	1.4	6.0	105	99	97	91	86	98
NOVO B	NOVO NORDISK A/S	Denmark		DEC	21,536.3	20,862.5	18,325.1	17,152.4	18,013.7	15,871.3	15,706.8	7.8	4.7	10.9	137	133	117	109	115	101
4528	ONO PHARMACEUTICAL CO., LTD.	Japan	#	MAR	0.0	2,796.4	2,717.6	2,604.8	2,465.4	2,195.5	1,426.5	8.6	14.0	5.8	0	196	191	183	173	154
4578	OTSUKA HOLDINGS CO., LTD.	Japan		DEC	13,012.9	13,786.1	12,847.6	11,775.8	11,008.6	10,240.2	12,023.5	3.2	4.6	5.3	108	115	107	98	92	85
PRGO	PERRIGO COMPANY PLC	Ireland		DEC	4,138.7	4,088.2	3,869.9	4,731.7	4,946.2	5,280.6	5,014.6	4.2	-4.8	1.2	83	82	77	94	99	105
PFE	PFIZER INC.	United States		DEC	81,288.0	41,651.0	40,905.0	40,825.0	52,546.0	52,824.0	48,851.0	2.9	9.0	95.2	166	85	84	84	108	108
RO	ROCHE HOLDING AG	Switzerland		DEC	72,234.8	68,203.4	65,825.2	60,466.9	57,201.2	51,818.3	50,342.1	4.1	4.6	9.1	143	135	131	120	114	103
SAN	SANOFI	France		DEC	44,552.5	45,711.3	42,229.8	40,848.4	43,493.0	36,626.2	37,861.5	1.1	2.5	4.8	118	121	112	108	115	97
4507	SHIONOGI & CO., LTD.	Japan	#	MAR	0.0	2,687.0	3,098.2	3,282.4	3,245.3	3,039.4	2,758.7	0.5	-0.8	-10.9	0	97	112	119	118	110
4502	TAKEDA PHARMACEUTICAL COMPAN	Japan	#	MAR	0.0	28,913.6	30,586.7	18,926.3	16,670.9	15,534.1	16,085.6	8.5	12.1	-2.8	0	180	190	118	104	97
UCB	UCB SA	Belgium		DEC	6,570.0	6,540.7	5,513.4	5,303.4	5,372.2	4,377.7	4,209.6	5.9	6.9	8.0	156	155	131	126	128	104
VIFN	VIFOR PHARMA AG	Switzerland		DEC	1,987.8	1,991.2	1,811.4	1,665.2	1,414.0	1,234.2	3,890.9	-6.2	7.6	2.9	51	51	47	43	36	32
ZTS	ZOETIS INC.	United States		DEC	7,776.0	6,675.0	6,260.0	5,825.0	5,307.0	4,888.0	4,765.0	6.3	9.7	16.5	163	140	131	122	111	103

Note: Data as originally reported. CAGR-Compound annual growth rate. #Of the following calendar year.
Companies are based on the constituents of the S&P Global 1200 Index.
Souce: S&P Capital IQ.

Net Income

Ticker	Company	Country		Yr. End	Million $ 2021	2020	2019	2018	2017	2016	2015	CAGR (%) 10-Yr.	5-Yr.	1-Yr.	Index Basis (2012=100) 2021	2020	2019	2018	2017	2016
PHARMACEUTICALS																				
4503	ASTELLAS PHARMA INC.	Japan	#	MAR	0.0	1,090.3	1,816.1	2,005.8	1,550.6	1,961.4	1,723.8	6.0	-9.0	-38.3	0	63	105	116	90	114
AZN	ASTRAZENECA PLC	United Kingdom		DEC	112.0	3,196.0	1,335.0	2,155.0	3,001.0	3,499.0	2,825.0	-36.1	-49.8	-96.5	4	113	47	76	106	124
BHC	BAUSCH HEALTH COMPANIES INC.	Canada		DEC	-948.0	-560.0	-1,788.0	-4,148.0	2,404.0	-2,409.0	-292.0	NA	-17.0	69.3	325	192	612	1421	-823	825
BAYN	BAYER AKTIENGESELLSCHAFT	Germany		DEC	1,137.3	-12,837.9	4,591.0	1,940.7	8,808.8	4,783.1	4,463.8	-8.6	-26.1	NM	25	-288	103	43	197	107
BMY	BRISTOL-MYERS SQUIBB COMPANY	United States		DEC	6,994.0	-9,015.0	3,439.0	4,920.0	1,007.0	4,457.0	1,565.0	6.5	9.4	NM	447	-576	220	314	64	285
WEED	CANOPY GROWTH CORPORATION	Canada	#	MAR	0.0	-1,387.2	-932.2	-550.9	-52.2	-5.6	-2.7	NA	246.5	32.1	0	51457	34579	20434	1935	209
CTLT	CATALENT, INC.	United States		JUN	585.0	221.0	137.0	83.6	109.8	111.5	212.2	NA	39.3	164.7	276	104	65	39	52	53
4519	CHUGAI PHARMACEUTICAL CO., LTD.	Japan		DEC	2,631.6	2,080.6	1,449.8	843.0	645.6	459.0	508.5	24.0	41.4	41.1	517	409	285	166	127	90
4568	DAIICHI SANKYO COMPANY, LIMITED	Japan	#	MAR	0.0	686.8	1,199.6	843.0	567.6	479.5	732.3	0.8	-1.6	-41.2	0	94	164	115	78	65
4523	EISAI CO., LTD.	Japan	#	MAR	0.0	380.8	1,131.6	572.0	488.2	353.0	488.9	-4.6	-5.2	-65.4	0	78	231	117	100	72
LLY	ELI LILLY AND COMPANY	United States		DEC	5,581.7	6,193.7	8,318.4	3,232.0	-204.1	2,737.6	2,408.4	2.5	15.3	-9.9	232	257	345	134	-8	114
GSK	GLAXOSMITHKLINE PLC	United Kingdom		DEC	5,937.6	7,849.1	6,151.9	4,617.6	2,070.7	1,126.0	12,420.0	-1.7	36.9	-23.7	48	63	50	37	17	9
JNJ	JOHNSON & JOHNSON	United States	#	JAN	0.0	20,878.0	15,119.0	15,297.0	1,300.0	1,300.0	16,540.0	8.0	4.8	41.9	0	126	91	92	8	8
MRK	MERCK & CO., INC.	United States		DEC	13,049.0	7,067.0	9,843.0	6,220.0	2,394.0	3,920.0	4,442.0	7.6	27.2	84.6	294	159	222	140	54	88
MRK	MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN	Germany		DEC	3,474.4	2,430.6	1,481.3	3,863.1	3,128.0	1,719.6	1,211.0	17.5	13.4	53.7	287	201	122	319	258	142
VTRS	VIATRIS INC.	United States		DEC	-1,269.1	-669.9	16.8	352.5	696.0	480.0	847.6	NA	NM	89.4	-150	-79	2	42	82	57
NOVN	NOVARTIS AG	Switzerland		DEC	24,021.0	8,072.0	11,732.0	12,611.0	7,703.0	6,712.0	17,783.0	10.2	29.0	197.6	135	45	66	71	43	38
NOVO B	NOVO NORDISK A/S	Denmark		DEC	7,304.7	6,925.0	5,849.7	5,924.7	6,149.4	5,384.8	5,073.2	10.8	4.7	13.3	144	137	115	117	121	106
4528	ONO PHARMACEUTICAL CO., LTD.	Japan	#	MAR	0.0	682.0	554.9	465.1	473.5	500.4	222.3	12.0	24.7	26.3	0	307	250	209	213	225
4578	OTSUKA HOLDINGS CO., LTD.	Japan		DEC	1,089.7	1,435.3	1,170.0	751.9	998.7	792.8	699.6	4.5	6.3	-15.3	156	205	167	107	143	113
PRGO	PERRIGO COMPANY PLC	Ireland		DEC	-68.9	-162.6	146.1	131.0	119.6	-4,012.8	-1.9	NA	-55.6	-57.6	3626	8558	NM	NM	NM	211200
PFE	PFIZER INC.	United States		DEC	21,979.0	9,159.0	16,026.0	11,153.0	21,308.0	7,215.0	6,960.0	8.2	25.0	140.0	316	132	230	160	306	104
RO	ROCHE HOLDING AG	Switzerland		DEC	15,280.7	16,157.1	13,936.1	10,671.2	8,858.4	9,427.2	8,852.3	4.1	7.8	-2.6	173	183	157	121	100	106
SAN	SANOFI	France		DEC	7,077.2	15,038.5	3,090.6	4,930.2	10,105.7	4,971.0	4,656.0	1.0	5.7	-49.4	152	323	66	106	217	107
4507	SHIONOGI & CO., LTD.	Japan	#	MAR	0.0	1,011.4	1,135.6	1,198.1	1,025.1	752.3	593.5	18.8	10.9	-8.5	0	170	191	202	173	127
4502	TAKEDA PHARMACEUTICAL COMPANY LIMITED	Japan	#	MAR	0.0	3,399.7	411.2	1,220.0	1,759.7	1,030.9	713.5	4.3	36.2	749.9	0	477	58	171	247	144
UCB	UCB SA	Belgium		DEC	1,203.2	895.4	888.8	916.0	904.2	548.9	676.6	16.1	15.3	44.5	178	132	131	135	134	81
VIFN	VIFOR PHARMA AG	Switzerland		DEC	158.4	406.4	164.3	154.9	1,177.0	233.3	300.7	-4.3	-9.4	-59.8	53	135	55	52	391	78
ZTS	ZOETIS INC.	United States		DEC	2,037.0	1,638.0	1,500.0	1,428.0	864.0	821.0	339.0	23.6	19.9	24.4	601	483	442	421	255	242

Note: Data as originally reported. CAGR-Compound annual growth rate. #Of the following calendar year.
Companies are based on the constituents of the S&P Global 1200 Index.
Souce: S&P Capital IQ.

					Return on Revenues (%)						Return on Assets (%)						Return on Equity (%)					
Ticker	**Company**	**Country**		**Yr. End**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**
PHARMACEUTICALS																						
4503	ASTELLAS PHARMA INC.	Japan	#	MAR	0.0	9.7	15.0	17.0	12.7	16.7	NA	5.3	8.4	11.7	8.9	12.0	0.0	9.0	15.3	17.6	13.0	17.3
AZN	ASTRAZENECA PLC	United Kingdom		DEC	0.3	12.0	5.5	9.8	13.4	15.2	0.1	4.8	2.2	3.6	4.7	5.6	0.4	20.8	8.6	13.4	17.2	19.4
BHC	BAUSCH HEALTH COMPANIES INC.	Canada		DEC	NM	NM	NM	NM	27.6	NM	NM	NM	NM	NM	6.4	NM	NM	NM	NM	NM	52.2	NM
BAYN	BAYER AKTIENGESELLSCHAFT	Germany		DEC	2.3	NM	9.4	4.6	21.0	13.0	0.8	NM	3.2	1.3	9.8	5.5	3.2	NM	5.2	3.3	9.4	13.1
BMY	BRISTOL-MYERS SQUIBB COMPANY	United States		DEC	15.1	NM	13.2	21.8	4.8	22.9	6.4	NM	2.6	14.1	3.0	13.2	19.0	NM	10.5	38.1	6.9	29.3
WEED	CANOPY GROWTH CORPORATION	Canada	#	MAR	0.0	NM	NM	NM	NM	NM	NA	NM	NM	NM	NM	NM	0.0	NM	NM	NM	NM	NM
CTLT	CATALENT, INC.	United States		JUN	14.6	7.1	5.4	3.4	5.3	6.0	6.4	2.8	2.2	1.8	3.2	3.6	15.0	7.6	8.1	9.2	16.2	17.4
4519	CHUGAI PHARMACEUTICAL CO., LTD.	Japan		DEC	30.3	27.3	23.0	16.0	13.6	10.9	19.7	17.4	14.9	10.1	8.5	6.6	28.0	23.4	19.6	12.8	11.0	8.5
4568	DAIICHI SANKYO COMPANY, LIMITED	Japan	#	MAR	0.0	7.9	13.1	10.0	6.3	5.6	NA	3.6	6.1	4.5	3.2	2.8	0.0	5.9	10.1	7.8	5.2	3.9
4523	EISAI CO., LTD.	Japan	#	MAR	0.0	6.5	17.5	9.9	8.6	7.3	NA	3.9	11.5	5.9	4.9	3.8	0.0	5.9	18.1	10.5	8.9	7.2
LLY	ELI LILLY AND COMPANY	United States		DEC	19.7	25.2	37.3	15.0	NM	12.9	11.4	13.3	21.2	7.4	NM	7.1	74.5	145.3	68.2	27.9	NM	19.1
GSK	GLAXOSMITHKLINE PLC	United Kingdom		DEC	12.9	16.9	13.8	11.8	5.1	3.3	5.5	7.1	5.8	6.2	2.7	1.5	24.2	32.6	47.8	113.0	51.3	15.3
JNJ	JOHNSON & JOHNSON	United States	#	JAN	0.0	22.3	17.8	18.4	18.8	1.7	NA	11.5	8.4	9.6	10.0	0.8	0.0	30.4	24.0	25.4	25.5	2.0
MRK	MERCK & CO., INC.	United States		DEC	26.8	17.0	25.2	14.7	6.0	9.8	12.3	7.7	11.7	7.5	2.7	4.1	38.8	17.6	21.2	20.2	6.5	9.3
MRK	MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN	Germany		DEC	15.5	11.3	8.2	22.7	17.9	10.8	6.7	4.8	3.0	9.1	7.3	4.3	15.9	11.4	7.4	7.0	18.2	12.1
VTRS	VIATRIS INC.	United States		DEC	NM	NM	0.1	3.1	5.8	4.3	NM	NM	0.1	1.1	1.9	1.4	NM	NM	0.1	2.8	5.7	4.6
NOVN	NOVARTIS AG	Switzerland		DEC	45.4	16.2	24.1	27.4	17.7	13.6	18.2	6.3	9.9	8.7	5.8	5.2	38.6	14.4	10.6	16.7	10.1	8.8
NOVO B	NOVO NORDISK A/S	Denmark		DEC	33.9	33.2	31.9	34.5	34.1	33.9	24.6	29.1	31.0	34.9	37.3	38.9	71.2	69.7	71.2	76.0	80.2	82.2
4528	ONO PHARMACEUTICAL CO., LTD.	Japan	#	MAR	0.0	24.4	20.4	17.9	19.2	22.8	NA	10.1	8.9	7.9	8.3	9.0	0.0	12.5	10.6	9.5	9.6	11.2
4578	OTSUKA HOLDINGS CO., LTD.	Japan		DEC	8.4	10.4	9.1	6.4	9.1	7.7	4.4	5.6	4.9	3.3	4.5	3.7	6.6	8.2	7.4	4.8	6.4	5.5
PRGO	PERRIGO COMPANY PLC	Ireland		DEC	NM	NM	3.8	2.8	2.4	NM	NM	NM	1.3	1.2	1.0	NM	NM	0.8	2.8	2.2	2.0	NM
PFE	PFIZER INC.	United States		DEC	27.0	22.0	39.2	27.3	40.6	13.7	12.1	5.9	9.6	7.0	12.4	4.2	31.9	10.5	16.9	5.7	32.5	11.6
RO	ROCHE HOLDING AG	Switzerland		DEC	21.2	23.7	21.2	17.6	15.5	18.2	15.1	16.6	16.2	13.4	11.3	12.5	43.9	39.8	42.6	36.6	31.9	39.2
SAN	SANOFI	France		DEC	15.9	32.9	7.3	12.1	23.2	13.6	5.2	10.7	2.4	3.9	8.4	4.5	9.5	20.1	4.9	7.5	6.7	7.7
4507	SHIONOGI & CO., LTD.	Japan	#	MAR	0.0	37.6	36.7	36.5	31.6	24.8	NA	11.2	14.0	17.0	15.1	12.5	0.0	13.8	17.0	20.9	19.2	16.1
4502	TAKEDA PHARMACEUTICAL COMPANY LIMITED	Japan	#	MAR	0.0	11.8	1.3	6.4	10.6	6.6	NA	2.9	0.3	1.0	4.6	2.6	0.0	7.6	0.9	3.8	9.4	5.8
UCB	UCB SA	Belgium		DEC	18.3	13.7	16.1	17.3	16.8	12.5	7.4	5.5	7.1	7.6	7.6	5.1	13.5	10.7	12.3	13.6	13.7	10.3
VIFN	VIFOR PHARMA AG	Switzerland		DEC	8.0	20.4	9.1	9.3	83.2	18.9	2.8	6.9	3.2	3.4	27.8	4.4	6.6	6.1	6.3	7.3	4.4	10.6
ZTS	ZOETIS INC.	United States		DEC	26.2	24.5	24.0	24.5	16.3	16.8	14.7	12.0	13.0	13.3	10.1	10.7	48.9	50.5	61.3	71.7	52.5	63.2

Note: Data as originally reported. CAGR-Compound annual growth rate. #Of the following calendar year.
Companies are based on the constituents of the S&P Global 1200 Index.
Souce: S&P Capital IQ.

					Current Ratio						Debt/Capital Ratio (%)						Debt as a % of Net Working Capital					
Ticker	**Company**	**Country**		**Yr. End**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**
PHARMACEUTICALS																						
4503	ASTELLAS PHARMA INC.	Japan	#	MAR	0.0	1.5	1.1	1.7	2.0	2.2	NA	13.7	25.5	0.1	0.3	0.0	NA	71.5	478.4	0.4	0.8	0.1
AZN	ASTRAZENECA PLC	United Kingdom		DEC	1.2	1.0	0.9	1.0	0.8	0.9	43.7	57.7	55.8	60.0	53.6	51.1	825.4	NM	NM	NM	NM	NM
BHC	BAUSCH HEALTH COMPANIES INC.	Canada		DEC	1.1	1.1	1.1	1.1	1.1	1.4	100.2	97.5	95.6	89.5	80.9	90.2	5,538.9	5,576.9	3,420.4	6,420.5	5,279.3	2,033.0
BAYN	BAYER AKTIENGESELLSCHAFT	Germany		DEC	1.1	1.0	1.4	1.3	2.2	1.6	51.7	51.3	43.1	44.7	25.0	33.1	1,119.7	NM	389.9	470.6	74.5	132.7
BMY	BRISTOL-MYERS SQUIBB COMPANY	United States		DEC	1.5	1.6	1.6	1.7	1.6	1.6	52.6	56.5	46.2	30.9	42.3	27.0	349.2	438.1	397.9	86.6	150.5	122.5
WEED	CANOPY GROWTH CORPORATION	Canada	#	MAR	0.0	10.0	6.1	11.9	5.2	10.1	NA	30.3	8.0	10.6	0.5	1.3	NA	61.6	20.9	18.7	1.8	5.4
CTLT	CATALENT, INC.	United States		JUN	2.4	2.6	2.1	2.1	2.3	2.0	41.2	44.4	54.3	70.9	74.0	74.2	173.8	200.2	374.5	399.4	347.9	459.3
4519	CHUGAI PHARMACEUTICAL CO., LTD.	Japan		DEC	8.0	3.5	3.9	4.4	4.9	4.7	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.1
4568	DAIICHI SANKYO COMPANY, LIMITED	Japan	#	MAR	0.0	3.6	3.9	3.6	3.4	3.7	NA	11.4	13.7	15.0	18.7	19.3	NA	17.9	19.8	21.9	30.7	32.2
4523	EISAI CO., LTD.	Japan	#	MAR	0.0	2.0	2.1	2.0	2.2	2.2	NA	6.4	7.3	13.3	21.8	21.3	NA	19.0	20.4	35.8	57.1	62.8
LLY	ELI LILLY AND COMPANY	United States		DEC	1.2	1.4	1.2	1.7	1.3	1.4	62.7	74.2	92.7	48.3	58.6	43.1	452.6	337.0	792.9	112.5	271.6	234.9
GSK	GLAXOSMITHKLINE PLC	United Kingdom		DEC	0.8	0.9	0.8	0.8	0.6	0.9	49.8	54.4	67.3	103.1	84.6	81.7	NM	NM	NM	NM	NM	NM
JNJ	JOHNSON & JOHNSON	United States	#	JAN	0.0	1.3	1.2	1.3	1.5	1.4	NA	30.4	34.9	30.9	31.8	36.4	NA	200.7	382.7	285.7	188.1	263.7
MRK	MERCK & CO., INC.	United States		DEC	1.3	1.0	1.2	1.2	1.3	1.8	44.7	58.1	50.2	53.9	38.3	38.0	481.7	6,748.5	464.5	686.7	348.9	183.2
MRK	MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN	Germany		DEC	1.1	1.0	0.8	1.1	0.9	0.8	30.1	39.6	35.2	31.9	43.6	45.9	1,604.4	21,377.6	NM	1,059.2	NM	NM
VTRS	VIATRIS INC.	United States		DEC	1.1	1.2	1.2	1.4	1.1	1.5	52.7	51.8	48.6	52.0	49.3	57.9	2,082.5	1,021.0	943.8	739.5	1,559.4	614.4
NOVN	NOVARTIS AG	Switzerland		DEC	1.5	0.9	1.0	1.2	1.2	1.1	29.2	40.5	33.2	28.5	28.7	25.3	170.9	NM	2,032.0	483.7	582.3	863.6
NOVO B	NOVO NORDISK A/S	Denmark		DEC	0.9	0.9	1.1	1.1	1.3	1.3	28.0	10.6	1.1	1.0	3.4	0.5	NM	NM	19.0	10.5	13.0	1.9
4528	ONO PHARMACEUTICAL CO., LTD.	Japan	#	MAR	0.0	2.6	2.5	2.3	3.1	3.3	NA	0.0	0.0	0.0	0.0	0.0	NA	0.0	0.0	0.0	0.1	0.0
4578	OTSUKA HOLDINGS CO., LTD.	Japan		DEC	2.2	2.4	2.2	2.2	2.6	2.6	4.8	6.2	7.1	8.8	10.0	12.1	17.7	21.2	24.9	32.5	31.9	34.5
PRGO	PERRIGO COMPANY PLC	Ireland		DEC	2.4	2.3	2.0	1.9	2.0	1.5	36.0	38.3	36.6	35.0	34.6	46.7	127.5	200.3	239.8	223.6	236.4	539.2
PFE	PFIZER INC.	United States		DEC	1.4	1.4	0.9	1.6	1.4	1.3	32.4	37.6	51.0	38.5	38.1	41.6	216.2	413.6	NM	206.7	374.4	485.2
RO	ROCHE HOLDING AG	Switzerland		DEC	0.9	1.3	1.3	1.4	1.4	1.3	37.3	23.6	29.0	35.9	37.0	44.0	NM	156.4	197.3	180.8	176.5	314.7
SAN	SANOFI	France		DEC	1.4	1.8	1.4	1.4	1.7	1.9	20.1	24.1	25.8	27.5	20.0	22.8	185.0	138.1	239.1	306.1	133.1	109.8
4507	SHIONOGI & CO., LTD.	Japan	#	MAR	0.0	5.6	6.4	5.2	5.4	3.8	NA	0.0	0.0	0.0	3.0	5.4	NA	0.0	0.0	0.0	5.8	11.9
4502	TAKEDA PHARMACEUTICAL COMPANY LIMITED	Japan	#	MAR	0.0	1.5	1.1	1.2	1.5	0.9	NA	47.1	48.9	52.9	32.8	39.4	NA	490.9	1,537.0	1,196.9	288.8	NM
UCB	UCB SA	Belgium		DEC	1.3	1.3	1.4	1.4	1.4	1.0	19.2	23.9	11.6	17.4	21.4	22.7	224.8	296.1	102.0	164.4	213.9	NM
VIFN	VIFOR PHARMA AG	Switzerland		DEC	1.9	3.0	2.6	2.1	1.9	0.5	1.9	11.8	12.6	12.5	3.4	68.0	8.4	50.7	62.3	73.3	23.4	NM
ZTS	ZOETIS INC.	United States		DEC	3.9	3.0	2.6	3.6	3.9	3.0	59.2	63.7	68.7	74.8	73.5	74.9	128.5	149.0	202.2	203.1	158.6	196.6

Note: Data as originally reported. CAGR-Compound annual growth rate. #Of the following calendar year.
Companies are based on the constituents of the S&P Global 1200 Index.
Souce: S&P Capital IQ.

Ticker	Company	Country		Yr. End	Price/Earnings Ratio (High-Low) 2021	2020	2019	2018	2017	2016	Dividend Payout Ratio (%) 2021	2020	2019	2018	2017	2016	Dividend Yield (High-Low, %) 2021	2020	2019	2018	2017	2016
PHARMACEUTICALS																						
4503	ASTELLAS PHARMA INC.	Japan	#	MAR	31 - 23	19 - 13	17 - 12	20 - 16	19 - 14	21 - 16	0.0	63.2	37.6	32.4	43.5	32.1	3.1 - 2.3	2.9 - 2.1	2.8 - 2.0	2.8 - 1.9	2.7 - 2.2	2.4 - 1.9
AZN	ASTRAZENECA PLC	United Kingdom		DEC	1625 - 1199	48 - 31	99 - 68	48 - 38	29 - 22	25 - 18	3442.9	111.8	269.1	161.7	117.3	101.8	2.6 - 2.2	3.0 - 2.2	3.7 - 2.4	4.0 - 2.9	4.4 - 3.4	5.5 - 4.0
BHC	BAUSCH HEALTH COMPANIES INC.	Canada		DEC	NM - NM	NM - NM	NM - NM	NM - NM	3 - 1	NM - NM	0.0	0.0	0.0	0.0	0.0	0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
BAYN	BAYER AKTIENGESELLSCHAFT	Germany		DEC	60 - 43	NM - NM	18 - 13	65 - 33	14 - 10	22 - 16	199.3	NM	63.8	141.7	30.4	45.6	4.5 - 3.3	6.0 - 3.5	6.9 - 3.6	5.3 - 3.8	4.6 - 2.5	2.9 - 2.2
BMY	BRISTOL-MYERS SQUIBB COMPANY	United States		DEC	22 - 17	NM - NM	32 - 21	23 - 16	107 - 76	29 - 18	62.9	NM	77.9	53.1	255.9	57.1	3.7 - 2.9	3.7 - 2.8	3.9 - 2.7	3.8 - 2.8	3.3 - 2.3	3.3 - 2.4
WEED	CANOPY GROWTH CORPORATION	Canada	#	MAR	NM - NM	NM - NM	NM - NM	NM - NM	NM - NM	NM - NM	0.0	0.0	0.0	0.0	0.0	0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
CTLT	CATALENT, INC.	United States		JUN	40 - 23	69 - 32	59 - 33	74 - 53	43 - 24	38 - 23	3.8	16.3	0.0	0.0	0.0	0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
4519	CHUGAI PHARMACEUTICAL CO., LTD.	Japan		DEC	35 - 19	43 - 24	35 - 22	44 - 31	45 - 24	45 - 32	32.5	42.6	35.8	37.9	41.3	59.1	2.6 - 2.2	2.5 - 0.8	1.5 - 0.9	1.3 - 0.8	1.2 - 0.8	1.7 - 1.0
4568	DAIICHI SANKYO COMPANY, LIMITED	Japan	#	MAR	105 - 59	40 - 21	33 - 23	43 - 24	36 - 28	22 - 15	0.0	64.4	35.1	48.5	77.0	82.1	1.4 - 0.8	1.3 - 0.7	1.7 - 0.9	2.1 - 1.4	3.1 - 1.7	3.2 - 2.2
4523	EISAI CO., LTD.	Japan	#	MAR	75 - 49	22 - 12	50 - 28	38 - 30	54 - 43	43 - 33	0.0	108.9	37.7	67.8	82.8	109.0	2.8 - 1.3	2.6 - 1.6	2.9 - 1.6	2.7 - 1.3	2.7 - 2.1	2.8 - 2.0
LLY	ELI LILLY AND COMPANY	United States		DEC	45 - 27	25 - 17	15 - 12	38 - 24	NM - NM	33 - 26	55.3	43.4	29.0	71.5	NM	78.8	1.7 - 1.3	2.2 - 1.2	2.5 - 1.8	2.4 - 1.9	3.0 - 1.9	3.1 - 2.4
GSK	GLAXOSMITHKLINE PLC	United Kingdom		DEC	18 - 14	15 - 10	19 - 15	22 - 18	52 - 40	97 - 79	91.2	69.2	85.1	108.4	255.0	425.5	5.4 - 4.7	6.7 - 5.0	6.2 - 4.3	5.6 - 4.5	6.4 - 4.9	6.3 - 4.6
JNJ	JOHNSON & JOHNSON	United States	#	JAN	21 - 14	27 - 23	26 - 21	26 - 20	260 - 208	17 - 15	0.0	52.8	71.2	65.6	62.1	687.9	2.7 - 2.4	3.4 - 2.5	3.0 - 2.6	3.0 - 2.3	2.9 - 2.3	3.1 - 2.6
MRK	MERCK & CO., INC.	United States		DEC	18 - 14	33 - 24	24 - 19	34 - 23	76 - 62	46 - 34	50.7	87.9	57.9	83.2	215.8	130.7	3.8 - 3.4	3.7 - 2.9	3.7 - 2.7	3.0 - 2.4	3.6 - 2.4	3.5 - 2.8
MRK	MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN	Germany		DEC	32 - 19	30 - 16	36 - 28	13 - 10	17 - 14	28 - 20	24.5	34.2	51.3	22.4	23.8	36.6	1.1 - 0.6	1.1 - 0.6	1.6 - 1.0	1.4 - 1.1	1.7 - 1.3	1.4 - 1.0
VTRS	VIATRIS INC.	United States		DEC	NM - NM	NM - NM	985 - 516	70 - 38	35 - 23	59 - 36	NM	0.0	0.0	0.0	0.0	0.0	4.9 - 3.0	3.6 - 2.7	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
NOVN	NOVARTIS AG	Switzerland		DEC	9 - 7	28 - 20	19 - 15	17 - 13	26 - 21	31 - 24	30.7	86.6	56.6	55.2	84.3	96.5	4.2 - 3.6	4.1 - 3.4	4.2 - 3.1	3.7 - 3.0	3.9 - 3.1	3.9 - 3.2
NOVO B	NOVO NORDISK A/S	Denmark		DEC	37 - 21	25 - 17	24 - 18	24 - 17	21 - 13	28 - 15	45.1	47.8	49.8	49.3	49.4	62.8	1.6 - 1.2	2.2 - 1.2	2.4 - 1.8	2.7 - 2.1	2.9 - 2.2	4.0 - 2.3
4528	ONO PHARMACEUTICAL CO., LTD.	Japan	#	MAR	24 - 16	22 - 15	35 - 22	34 - 22	55 - 21	99 - 48	0.0	29.8	38.1	42.4	46.6	36.1	2.3 - 1.5	2.4 - 1.3	2.4 - 1.7	2.1 - 1.2	1.8 - 1.3	1.7 - 0.6
4578	OTSUKA HOLDINGS CO., LTD.	Japan		DEC	23 - 18	18 - 11	21 - 15	38 - 29	27 - 21	33 - 21	44.6	0.0	0.0	67.0	48.8	59.1	2.6 - 2.3	2.5 - 2.0	3.1 - 2.0	2.9 - 1.8	2.2 - 1.7	2.3 - 1.7
PRGO	PERRIGO COMPANY PLC	Ireland		DEC	NM - NM	NM - NM	53 - 36	100 - 38	106 - 79	NM - NM	NM	NM	76.9	80.1	76.2	NM	3.0 - 2.3	2.7 - 1.8	2.2 - 1.4	2.1 - 1.2	1.3 - 0.7	1.0 - 0.7
PFE	PFIZER INC.	United States		DEC	16 - 9	26 - 17	15 - 12	24 - 18	10 - 9	31 - 24	39.7	92.1	50.2	71.5	35.9	101.4	3.5 - 2.6	4.7 - 2.9	5.3 - 3.7	4.2 - 3.0	4.0 - 2.9	4.1 - 3.5
RO	ROCHE HOLDING AG	Switzerland		DEC	23 - 18	20 - 15	20 - 15	21 - 17	27 - 22	25 - 20	55.8	53.9	55.2	67.6	81.1	72.1	2.7 - 2.4	3.1 - 2.4	3.3 - 2.5	3.5 - 2.8	4.0 - 3.2	3.7 - 3.0
SAN	SANOFI	France		DEC	19 - 16	9 - 6	41 - 33	23 - 19	13 - 10	23 - 19	64.4	32.0	139.2	87.6	44.1	79.8	3.8 - 3.4	4.2 - 3.5	4.3 - 3.3	4.2 - 3.6	4.8 - 3.8	4.0 - 3.2
4507	SHIONOGI & CO., LTD.	Japan	#	MAR	20 - 14	18 - 11	18 - 13	18 - 15	25 - 18	27 - 18	0.0	29.1	25.5	20.8	22.3	26.4	2.0 - 1.3	2.3 - 1.5	1.8 - 1.2	1.6 - 1.1	1.4 - 1.1	1.5 - 1.1
4502	TAKEDA PHARMACEUTICAL COMPANY LIMITED	Japan	#	MAR	18 - 13	160 - 100	42 - 25	27 - 21	38 - 30	58 - 47	0.0	75.4	638.7	105.7	75.9	123.3	6.0 - 4.2	6.2 - 4.3	5.2 - 3.7	5.0 - 3.0	3.5 - 2.7	4.4 - 3.2
UCB	UCB SA	Belgium		DEC	19 - 14	28 - 14	19 - 15	19 - 15	18 - 13	32 - 20	22.7	32.1	28.8	27.8	28.8	44.4	1.5 - 1.2	1.7 - 1.2	2.0 - 1.1	1.9 - 1.5	1.9 - 1.5	2.0 - 1.5
VIFN	VIFOR PHARMA AG	Switzerland		DEC	73 - 46	31 - 17	73 - 41	81 - 44	7 - 5	44 - 27	89.9	36.0	81.5	85.0	11.3	49.2	1.9 - 1.2	1.9 - 1.4	2.0 - 1.1	2.0 - 1.1	1.7 - 1.0	2.1 - 1.5
ZTS	ZOETIS INC.	United States		DEC	57 - 34	51 - 27	42 - 26	32 - 24	41 - 30	32 - 24	23.3	23.2	20.9	17.0	23.8	22.9	0.7 - 0.4	0.7 - 0.4	0.9 - 0.5	0.8 - 0.5	0.7 - 0.5	0.8 - 0.6

Note: Data as originally reported. CAGR-Compound annual growth rate. #Of the following calendar year.
Companies are based on the constituents of the S&P Global 1200 Index.
Souce: S&P Capital IQ.

					Earnings per Share ($)						Tangible Book Value per Share ($)						Share Price (High-Low, $)					
Ticker	Company	Country		Yr. End	2021	2020	2019	2018	2017	2016	2021	2020	2019	2018	2017	2016	2021	2020	2019	2018	2017	2016
PHARMACEUTICALS																						
4503	ASTELLAS PHARMA INC.	Japan	#	MAR	0.0	0.6	1.0	1.0	0.8	0.9	0.0	2.2	1.4	2.9	3.0	3.1	17.6 - 13.6	19.3 - 13.6	17.6 - 12.5	18.7 - 12.5	15.0 - 11.8	15.2 - 11.6
AZN	ASTRAZENECA PLC	United Kingdom		DEC	0.1	2.4	1.0	1.7	2.4	2.8	-14.9	-13.1	-14.8	-16.7	-18.2	-19.3	128.9 - 91.2	138.2 - 80.2	103.6 - 70.4	82.0 - 57.9	74.6 - 55.9	68.0 - 45.4
BHC	BAUSCH HEALTH COMPANIES INC.	Canada		DEC	-2.6	-1.6	-5.1	-11.8	6.8	-6.9	-54.3	-59.0	-63.1	-64.1	-71.6	-90.6	34.8 - 20.9	30.4 - 11.2	32.0 - 18.5	28.5 - 14.4	22.8 - 8.3	105.9 - 13.0
BAYN	BAYER AKTIENGESELLSCHAFT	Germany		DEC	1.2	-13.1	4.7	2.1	10.1	5.7	-33.6	-33.6	-24.3	-29.4	16.4	1.4	65.7 - 49.9	95.8 - 48.8	83.4 - 58.4	126.2 - 66.8	148.8 - 118.4	119.6 - 88.1
BMY	BRISTOL-MYERS SQUIBB COMPANY	United States		DEC	3.1	-4.0	2.0	3.0	0.6	2.7	-12.4	-16.0	-15.5	3.9	2.2	4.7	69.8 - 53.2	68.3 - 45.8	64.8 - 42.5	70.1 - 46.9	66.1 - 46.0	77.1 - 49.0
WEED	CANOPY GROWTH CORPORATION	Canada	#	MAR	0.0	-3.7	-2.7	-2.1	-0.3	0.0	0.0	2.7	4.9	10.5	2.9	1.1	56.6 - 8.7	30.0 - 10.2	54.7 - 14.1	56.2 - 15.3	26.4 - 5.2	13.3 - 1.8
CTLT	CATALENT, INC.	United States		JUN	3.1	1.1	0.9	0.6	0.9	0.9	3.4	-2.8	-10.1	-6.4	-4.7	-5.2	142.6 - 97.9	120.5 - 31.0	58.4 - 29.3	47.9 - 29.2	43.4 - 25.5	32.2 - 18.9
4519	CHUGAI PHARMACEUTICAL CO., LTD.	Japan		DEC	1.6	1.3	0.9	0.5	0.4	0.3	6.2	5.6	4.7	4.1	3.6	3.3	55.9 - 30.3	57.8 - 30.7	31.7 - 18.9	23.8 - 15.4	17.8 - 9.7	12.0 - 8.6
4568	DAIICHI SANKYO COMPANY, LIMITED	Japan	#	MAR	0.0	0.4	0.6	0.4	0.3	0.2	0.0	4.8	5.1	4.7	4.3	4.0	32.6 - 17.2	38.3 - 16.8	23.2 - 10.5	15.3 - 9.1	8.8 - 6.8	7.9 - 5.9
4523	EISAI CO., LTD.	Japan	#	MAR	0.0	1.3	3.9	2.0	1.7	1.2	0.0	13.3	13.1	11.3	10.6	9.3	110.9 - 55.8	105.6 - 58.9	89.1 - 47.9	104.7 - 49.2	63.5 - 48.8	68.9 - 46.0
LLY	ELI LILLY AND COMPANY	United States		DEC	6.1	6.8	8.9	3.1	-0.2	2.6	-2.9	-6.1	-8.5	7.3	3.0	5.4	283.9 - 161.8	173.9 - 117.1	137.0 - 101.4	119.8 - 73.7	89.1 - 73.5	85.4 - 64.2
GSK	GLAXOSMITHKLINE PLC	United Kingdom		DEC	1.2	1.6	1.2	0.9	0.4	0.2	-6.9	-7.1	-8.1	-5.0	-6.5	-6.0	22.1 - 16.1	25.4 - 17.5	24.5 - 18.9	21.0 - 15.0	23.3 - 17.2	21.6 - 16.2
JNJ	JOHNSON & JOHNSON	United States	#	JAN	0.0	7.8	5.5	5.6	5.6	0.5	0.0	-2.9	-10.1	-8.3	-6.9	-9.3	179.9 - 151.5	157.7 - 109.2	147.8 - 125.0	149.0 - 118.6	144.4 - 110.8	126.1 - 94.3
MRK	MERCK & CO., INC.	United States		DEC	5.1	2.8	3.8	2.3	0.9	1.4	-2.4	-3.0	-3.0	-1.8	0.7	1.7	91.4 - 70.9	92.1 - 65.3	92.6 - 72.1	80.2 - 52.8	66.8 - 53.6	65.5 - 48.0
MRK	MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN	Germany		DEC	8.0	5.6	3.4	8.9	7.2	4.0	-8.6	-18.8	-21.9	-10.0	-21.8	-26.7	263.3 - 144.0	171.7 - 93.2	123.8 - 96.3	114.7 - 85.3	138.3 - 104.7	106.0 - 74.6
VTRS	VIATRIS INC.	United States		DEC	-1.1	-1.1	0.0	0.7	1.3	0.9	-14.7	-15.8	-18.1	-21.8	-23.2	-23.5	18.8 - 12.0	23.1 - 12.8	32.2 - 16.6	47.8 - 26.0	45.9 - 29.4	54.4 - 33.6
NOVN	NOVARTIS AG	Switzerland		DEC	10.6	3.5	5.1	5.4	3.3	2.8	4.2	-2.4	2.5	8.5	7.6	7.1	95.3 - 80.1	108.9 - 73.6	99.3 - 79.5	94.3 - 73.0	87.6 - 71.3	85.6 - 66.0
NOVO B	NOVO NORDISK A/S	Denmark		DEC	3.2	3.0	2.5	2.4	2.5	2.1	1.9	3.0	3.3	3.0	3.1	2.4	118.3 - 63.9	76.9 - 54.5	59.2 - 44.4	54.4 - 40.7	54.8 - 36.4	57.7 - 31.0
4528	ONO PHARMACEUTICAL CO., LTD.	Japan	#	MAR	0.0	1.4	1.1	0.9	0.9	0.9	0.0	10.2	9.2	8.7	8.6	8.0	28.4 - 20.5	33.2 - 17.8	23.2 - 16.8	31.3 - 19.4	24.2 - 19.4	50.4 - 19.8
4578	OTSUKA HOLDINGS CO., LTD.	Japan		DEC	2.0	2.6	2.2	1.4	1.8	1.5	19.1	20.2	17.2	15.8	17.8	16.3	43.5 - 34.8	50.0 - 31.2	46.7 - 31.6	53.2 - 39.5	52.3 - 38.1	44.0 - 29.7
PRGO	PERRIGO COMPANY PLC	Ireland		DEC	-0.5	-1.2	1.1	1.0	0.8	-28.0	0.0	0.5	-9.6	-9.0	-9.8	-11.2	50.9 - 35.3	63.9 - 40.0	57.5 - 38.4	95.9 - 36.3	91.7 - 63.7	152.4 - 79.7
PFE	PFIZER INC.	United States		DEC	3.9	1.6	2.8	1.9	3.5	1.2	0.5	-2.6	-3.4	-4.4	-5.6	-7.8	61.7 - 33.4	43.1 - 27.9	44.6 - 34.0	46.5 - 33.2	37.4 - 30.9	37.4 - 28.3
RO	ROCHE HOLDING AG	Switzerland		DEC	17.8	18.7	16.1	12.4	10.3	11.0	2.1	20.0	14.2	11.1	9.6	0.7	421.5 - 321.5	404.5 - 300.4	328.2 - 250.2	264.6 - 209.7	280.1 - 232.0	273.0 - 214.9
SAN	SANOFI	France		DEC	5.6	11.9	2.5	3.9	8.0	3.8	6.3	6.4	0.3	-2.3	5.9	6.4	103.7 - 85.2	117.2 - 82.8	102.8 - 80.5	92.1 - 72.0	111.6 - 86.3	83.5 - 66.0
4507	SHIONOGI & CO., LTD.	Japan	#	MAR	0.0	3.3	3.7	3.8	3.2	2.3	0.0	22.8	21.6	17.8	15.8	12.1	73.3 - 46.7	69.6 - 42.4	66.3 - 50.6	71.1 - 47.4	57.4 - 47.4	54.0 - 35.8
4502	TAKEDA PHARMACEUTICAL COMPANY LIMITED	Japan	#	MAR	0.0	2.2	0.3	1.3	2.2	1.3	0.0	-16.0	-20.6	-22.1	-0.6	-2.2	37.9 - 26.0	43.9 - 28.0	44.4 - 31.3	61.0 - 31.9	57.5 - 41.4	51.7 - 35.1
UCB	UCB SA	Belgium		DEC	6.2	4.6	4.6	4.9	4.8	2.9	0.3	-4.3	6.7	2.7	0.9	-2.8	122.1 - 84.5	140.0 - 73.6	89.8 - 69.9	93.3 - 68.8	94.9 - 67.9	89.9 - 57.9
VIFN	VIFOR PHARMA AG	Switzerland		DEC	2.4	6.2	2.5	2.4	18.1	3.6	18.7	19.4	11.7	5.9	6.7	-19.3	179.7 - 112.2	214.7 - 109.6	186.5 - 105.1	195.3 - 105.3	134.1 - 96.4	156.0 - 94.2
ZTS	ZOETIS INC.	United States		DEC	4.3	3.4	3.1	2.9	1.8	1.7	0.8	-1.3	-3.7	-5.0	-2.1	-2.5	249.3 - 141.4	176.6 - 90.1	133.7 - 81.4	96.6 - 70.2	73.6 - 52.0	54.2 - 38.3

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