CFRA

Industry Surveys

Biotechnology

SEPTEMBER 2022

Stewart Glickman, CFA
Equity Analyst

Siti Salbiah
Industry Analyst

CONTENTS

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

Raymond Jarvis
Senior Editor

Atifi Kuddus, Geraldine Tan
Associate Editors

Marc Bastow
Contributing Editor

Copyright © 2022
CFRA
977 Seminole Trail, PMB 230
Charlottesville, VA 22901
All rights reserved.

CHARTS & FIGURES

NEW THEMES

What's Changed: In an effort to curb inflation in the U.S., the Inflation Reduction Act 2022 was recently enacted in August, which consists of an extensive package of health, tax, and climate change provisions. Head to page 15 for a breakdown of how the Act affects the Biotechnology industry –specifically, drug prices.

What's Changed: For biopharmaceutical companies, patents are crucial benchmarks of progress for new biotech products. Patents also often lead to feuds among biopharma players when it comes to infringements. Details on ongoing patent feuds on pages 23.

EXECUTIVE SUMMARY

CFRA has a neutral outlook on the Biotechnology industry. Here are current trends and the key themes that we see for the future.

The Market for Covid-19 Vaccines and Treatments is Becoming Saturated

Since late 2019 and the first outbreak of Covid-19, many biopharmaceutical companies have put forth efforts to develop and commercialize therapies for Covid-19. Successful companies quickly experienced the positive effects of Covid-19 treatments on their sales and profitability. For example, Gilead's treatment Veklury contributed 16% of total product sales as of the second quarter of 2022. Meanwhile, Moderna, which developed the second FDA-authorized Covid-19 vaccine, saw sales 9% increase year-over-year to $4.7 billion in the second quarter of 2022. There are now numerous treatments and vaccines being marketed globally, and there are still more to come. The market for Covid-19 therapeutics is becoming quite crowded, in our view. In the long run, we expect these vaccines to remain regular contributors to revenues as the disease moves into an 'endemic' phase. However, recent uptake of new market entrants, such as Nuvaxovid, has been underwhelming, which does not bode well for late-to-market arrivals.

Inflation Reduction Act Puts Drug Prices in the Crosshairs

The surprise August 2022 passage of the Inflation Reduction Act sets the stage for a novel change in drug pricing that could be significant in a few years. While the Act does not have any teeth to it until 2026 (when pricing changes go into effect), and while it only starts with 10 drugs yet-to-be-named, we believe that the important part is the structure. A list of 10 drugs will subsequently become 20 drugs and raises the possibility it could be expanded further. The bottom line, in our view, is that highly successful drugs could see their upside potential muted, to a degree, by a new pricing mechanism that brings down prices before generic competition actually begins.

M&A Activity Continues to be Robust

Mega M&A deals continued despite the pandemic, as major drugmakers remained eager as ever to find new avenues of growth to make up for sales of blockbuster drugs lost to patent expirations. This is aided by the industry's debt level, which remains low relative to historical levels. In addition, the pandemic has seemingly brought industry collaboration to an all-time high, leading us to believe that the M&A environment is favorable. In the past few years, we've seen significant M&A activity in immunology and oncology, which Evaluate forecasts to be two of the fastest growing therapeutic areas through 2026. The top 10 largest biopharmaceutical M&A deals in 2021 reached approximately $53 billion, primarily contributed by oncology, rare disease, and immunology/inflammation fields. Going forward, we expect interest in these therapeutic areas to remain high.

How Friendly is the FDA?

Lately, the FDA appears to be quite cooperative with the biopharmaceutical industry, as evidenced by lower times to approval and robust approval activity. The controversial June 2021 approval of aducanumab for Alzheimer's disease certainly convinced investors of the FDA's friendly stance as biotech stocks appreciated substantially across the board; however, there was significant public pushback against the approval that has led to congressional investigations. There has also been evidence of a tougher FDA as the agency required new and updated safety warnings and restricted the usage of JAK inhibitors, such as Pfizer's Xeljanz, AbbVie's Rinvoq, and Eli Lilly's Olumiant, due to increased risk of heart-related issues.

BIOTECHNOLOGY

Outlook: Neutral

MARKET CAP BREAKDOWN*

RANK NO.	COMPANY NAME	MARKET CAP ($ billion)
1	AbbVie	249.7
2	Amgen	121.4
3	Gilead Sciences	78.1
4	Vertex	71.0
5	Regeneron	73.3
	Others†	79.7

Source: CFRA, S&P Global Market Intelligence.
**Data as of September 27, 2022.*
†Refer to the "Comparative Company Analysis" section of this survey for the list of companies.

ETF FOCUS

IBB iShares Nasdaq Biotechnology	AUM ($M) 7,945.0	Expense Ratio 0.45
XBI SPDR S&P Biotech	AUM ($M) 7,466.3	Expense Ratio 0.35
BBH VanEck Vectors Biotech	AUM ($M) 440.1	Expense Ratio 0.35

BY THE NUMBERS

276 Vaccines in development for Covid-19 as of August 19, 2022

332 Treatments in development for Covid-19 as August 19, 2022

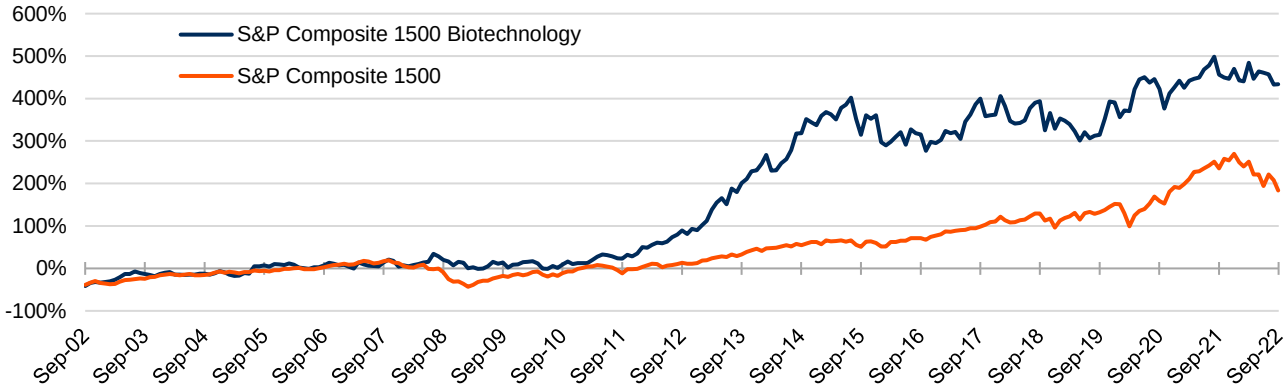
109 million Number of Americans have received Covid-19 boosters as of early September 2022

59 Number of drugs approved by the FDA in 2021, above prior 10-year average of 48

6.1% 2022-2026 CAGR for worldwide biosimilars market

3.3% Average drug price increase in 2021 vs. 5.8% in 2020

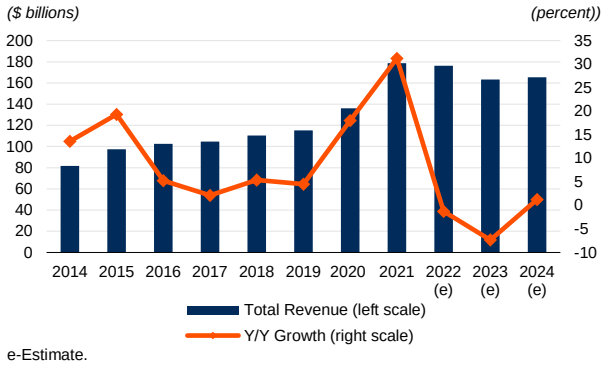
20-YEAR INDEX PERFORMANCE*



*Data as of September 27, 2022.
Source: S&P Global Market Intelligence.

FINANCIAL METRICS

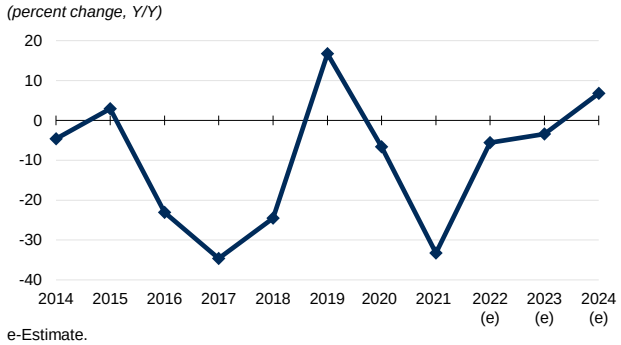
Revenue Growth



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

- We project revenue for the S&P Composite 1500 Biotechnology index to dampen by -1.3% in 2022, down from the 31.2% growth in 2021, and to further decelerate to -7.3% in 2023. We expect revenue growth to stabilize in 2024.
- The high revenue growth in 2021 was attributed to the rapid growth of drugs approved in the last several years and sales boost from Covid-19 vaccines and treatments.
- The potential weak revenue growth in 2023 is primarily driven by drop in sales of Covid-19 vaccines amid the endemic stage and a couple of expected patent expirations that year. In addition, strong foreign exchange headwinds in the first half of 2022 have been a factor, hurting revenues by 3%-5% per firm, on average.

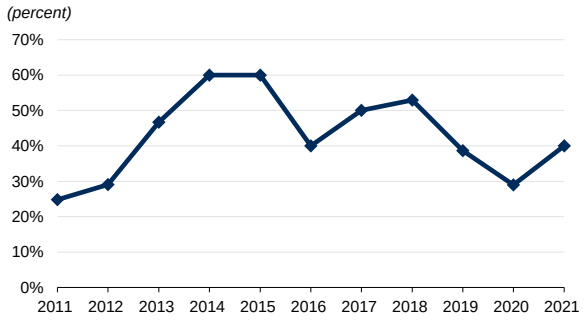
Median EPS Growth



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

- We anticipate that the median EPS growth rate for the industry will reach -5.6% in 2022 from a plunge of -33.3% in 2021.
- We estimate the median EPS growth rate to grow to -3.4% in 2023 and 6.8% in 2024, as the companies in the industry gradually return to profitability.
- The industry's earnings are likely to be affected by the introduction of new drugs, the ramp-up in sales of said drugs (sales tend to peak 5-7 years after launch), the strength of pricing pressures, and the decline in sales of mature drugs (typically due to the loss of marketing exclusivity).

Net Debt/Capitalization

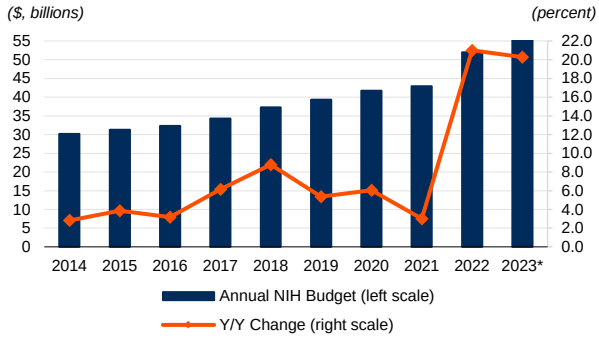


Source: CFRA, S&P Global Market Intelligence.

- The industry's net debt to capital ratio stood at 40% in 2021, slightly lower than average historical levels of 50%, reflecting strong M&A activity in the past few years.
- Looking forward, we foresee a potential cutback in M&A activity for the industry due to rising interest rates and weakening economic conditions.
- Many large-cap drug companies continue to seek new sources of long-term revenue growth as their blockbuster drugs face growing competition.

KEY INDUSTRY DRIVERS

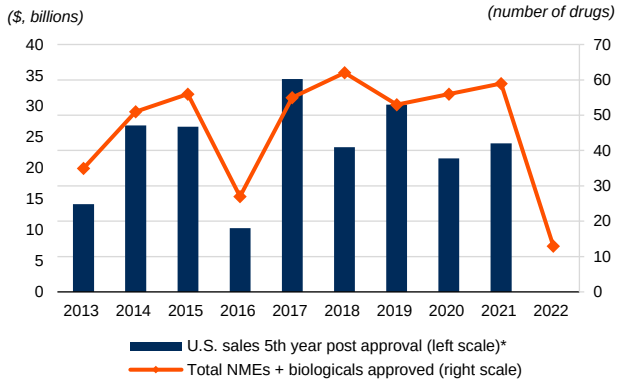
Annual NIH Budget



*Pending budget approval.
Source: National Institute of Heatlh.

- Spending by the National Institutes of Health (NIH) is key to biotech funding and innovation.
- In March 2022, President Biden proposed to the U.S. Congress a 20.3% increase in the NIH budget, amounting to $62.5 billion for the 2023 financial year. (The U.S. fiscal year runs from October 1 to September 30.)

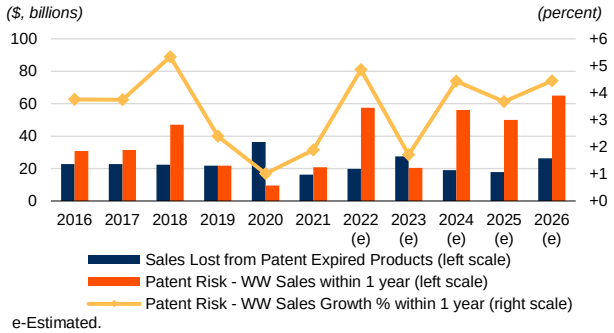
Drug Approvals in the U.S.



*Latest availabe data as of 2021.
Source: Evaluate.

- In 2021, the FDA approved 59 new molecular entities (NMEs), up from 58 approved in 2020. As of the second quarter of 2022, 13 drugs have been approved so far.
- Although a number of drug applications encountered some decision delays in 2021, the total number of drugs approved was well above the 10-year average of 48.
- The 5th year sales expectations for drugs approved in recent years are encouraging for the long-term growth of the biopharmaceutical industry.

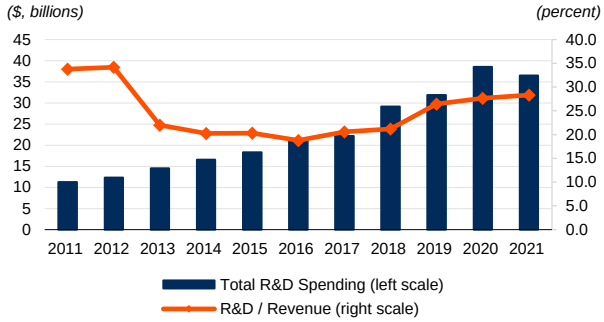
Worldwide Sales at Risk from Patent Expiration



e-Estimated.
Source: Evaluate.

- In 2021, the drug industry benefited from a low amount of drug sales at risk from patent expirations. In 2022 and 2023, we expect to see a marked increase in sales at risk. However, it is likely that the market has long anticipated the potential for lost sales.
- It is not uncommon for expectations around patent expirations to change due to patent litigation or patent extensions.

Aggregate R&D Spending*



*Constituents in the S&P Composite 1500 Biotechnology index.
Source: CFRA, S&P Global Market Intelligence.

- R&D spending by companies in the S&P Composite 1500 Biotechnology index has grown recently, boosted by significant acquisition activity.
- Looking ahead, Evaluate expects global R&D spending to grow at a CAGR of 4.2% from 2021 to 2026 – slower than revenue growth of 6.4% – as companies direct less of their revenue toward R&D (or achieve higher R&D efficiency).

INDUSTRY TRENDS

Competitive Environment

The Biopharmaceutical Industry Rapidly Mobilized to End the Pandemic

The novel coronavirus (Covid-19) pandemic, which began with an outbreak in China in December 2019, rapidly shifted the biopharmaceutical industry's priorities. In early 2020, many companies began efforts and reallocated resources to research and develop therapies for Covid-19. As of August 23, 2022, more than 599 million cases of Covid-19 have been reported globally, resulting in over 6.5 million deaths. The U.S. has authorized the use of three Covid-19 vaccines, which are mRNA-1273 (by Moderna), Comirnaty (by Pfizer and BioNTech), and Johnson & Johnson's vaccine. mRNA-1273 and Comirnaty are both mRNA vaccines, a novel technology. A number of biopharmaceutical companies are in the midst of developing Covid-19 treatments, with Gilead's Remdesivir currently approved by the FDA. According to the Milken Institute, as of August 19, 2022, there are still 332 treatments in development for Covid-19 and 276 vaccines in development. The FDA has authorized the inoculation of Covid-19 vaccine boosters manufactured by Pfizer, Moderna, Novavax, and Johnson & Johnson in the U.S, with 109 million Americans having received Covid-19 boosters as of early September 2022. In the future, Covid-19 could be treated more like the flu, with one annual shot offering year-long protection against severe illness. Looking forward, we expect biotechnology companies' focus will shift towards the Covid-19 boosters' market as well as non-related Covid-19 biotech business, as the Covid-19 vaccines sales gradually diminish as the world approaches the endemic stage.

As for normal biotech business, the impact of Covid-19 has so far been immaterial to both the supply and demand side of things for biotech firms. Covid-19 has certainly caused delays in clinical trials, but most trials have resumed, and we think these delays are immaterial to near-term revenues and long-term outlooks. The pandemic did not significantly impact the timing of FDA reviews for therapies unrelated to Covid-19, as we have not yet seen any significant delays of approval by the FDA.

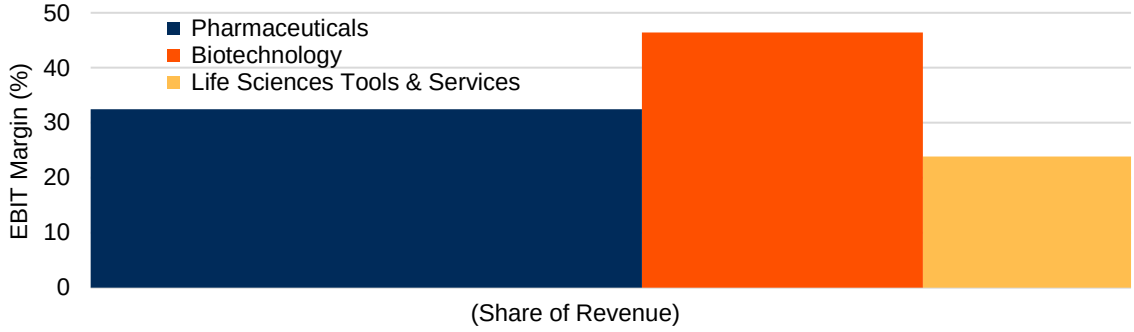
Biosimilar Progress Remains Slow in the U.S.

Biosimilars are near copies of branded biologic drugs that have shown no clinically meaningful difference from their reference products. U.S. legislators originally hoped that biosimilars could alleviate drug costs in the same way that generic drugs have lowered costs for traditional pharmaceuticals.

However, makers of branded biologic drugs have often retained significant market share despite the approval of biosimilars or alternative therapies because sizable development, manufacturing, and commercialization costs deter potential entrants. Biosimilar manufacturers may not be able to aggressively offer discounts because of their need to recoup costs that are much higher on average than those required to successfully bring a generic drug to market. Other reasons holding back the uptake of biosimilars include the slow regulatory process, defensive strategies of drug innovator companies (*e.g.*, extensive patent litigation), lack of an interchangeability designation in the U.S., and insufficient patient and physician education about the safety and efficacy of biosimilars.

As demonstrated in the profit share map on the next page, established biotech companies have high operating margins; however, the chart does not reflect the upfront development costs that are required for many years before any revenue is generated, nor the many failed therapies and companies.

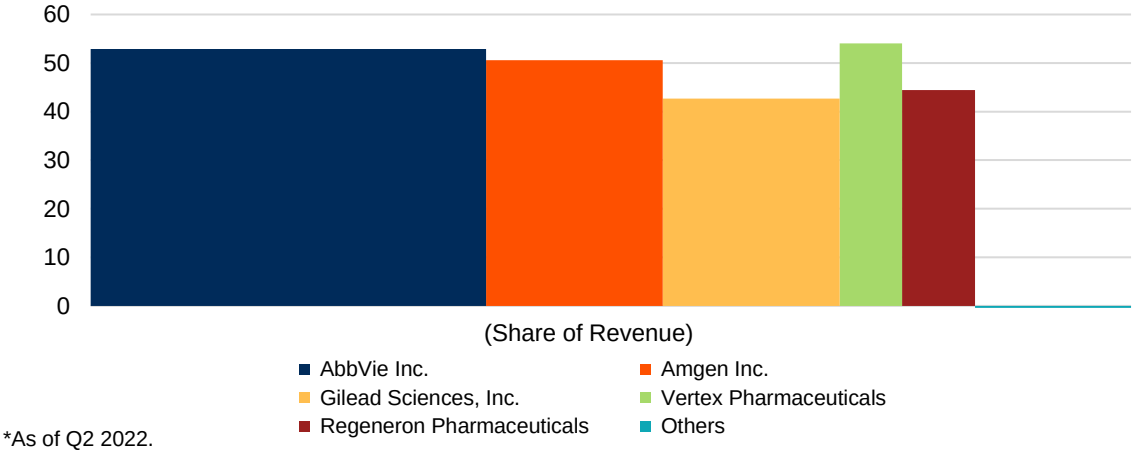
PROFIT SHARE MAP OF THE PHARMACEUTICALS, BIOTECHNOLOGY & LIFE SCIENCES INDUSTRIES
(5-year average)



Source: CFRA; S&P Global Market Intelligence.

Within the Biotechnology industry, AbbVie Inc. contributed the most in terms of revenue (38.4%) with an operating margin of (52.9%).

PROFIT SHARE MAP OF THE BIOTECHNOLOGY INDUSTRY*
(EBIT Margin, in percent)



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

PORTER'S FIVE FORCES

Although the biotech industry has fierce competition, immense barriers to entry, and a constant threat of substitution, firms are still enticed to compete in the industry because of the alluring potential for extremely high profits. As a result, the Biotechnology industry has become notorious for the many companies that go bankrupt and the few companies that reach astronomical valuations without having sold anything. Companies that have a commercially successful first product are often able to use the cash flows from that first product to support new and existing R&D efforts, eventually leading to the establishment of multiple, diverse revenue streams.

Power of Buyers (Moderate) - In the Biotechnology industry, end consumers have little to no negotiating power. Negotiating power typically lies somewhere in the supply chain, either with third-party payers (typically, health insurers and government programs), pharmacy benefit managers (PBMs that manage drug lists available to patients), or pharmacies. Third-party payers typically determine how much, if any, reimbursement is supplied for dispensed drugs. If a drug is too expensive, private third-party payers can typically deny reimbursement. Medicare, a government health program, has limited to no negotiating power for certain classes of drugs that have been designated as protected. Meanwhile, PBMs design

formularies, which are official lists of medicines that may be prescribed by health care providers or services. For drugs with limited or no competition (*e.g.*, still under exclusivity period or no other therapies are available), power of buyers is typically weak.

Power of Suppliers (Unique) - The raw materials and equipment used in biotechnology can often come from multiple suppliers. Much of the equipment and materials used by biotech companies may be easily sourced, meaning suppliers hold little power. However, the power of suppliers may be moderate to high in situations where biotech firms require the latest life science tools, equipment, or manufacturing processes. Many tools and equipment may require significant training before researchers can use them proficiently. This training and integration make it harder for biotech firms to switch to a different instrument supplier. Many biotech firms, especially less mature ones, rely on third parties to manufacture their drugs because it is more expensive to manufacture the drugs themselves. These third-party manufacturers can have significant negotiating power.

Barriers to Entry (High) - It is extremely difficult to enter the biotechnology market for a plethora of reasons. It is a highly regulated market in which it is difficult for new entrants to gain a thorough understanding of the regulatory processes and requirements. Biotech companies typically require significant upfront investment and may not achieve commercial success for many years. Companies often spend many years developing drug candidates that do not have commercial application. In addition, established firms aggressively defend their intellectual property with patent litigation and other strategies. Established firms also negotiate contracts with distributors, pharmacy benefit managers, and third-party payers in ways that make it nearly impossible for new entrants to compete.

Threat of Substitutes (Unique) - A newly approved drug typically has patent protection and exclusivity rights for years, meaning that substitutes often have little to no power. However, biotech companies can face many substitutes, primarily in the form of small molecule traditional drugs, non-biopharmaceutical technologies, and biosimilar products. Small molecule drugs are the drugs that have traditionally comprised a substantial proportion of the sales of pharmaceutical manufacturers. Non-biopharmaceutical technologies include medical devices and other technologies that can treat or alleviate health issues. Biosimilars are biologic products that are almost identical copies of branded biologic products (often, a drug). Biotech companies also face substitution in the form of other biotechnologies. We have seen the rise of new biotechnologies in recent years, such as gene therapy and mRNA therapeutics, and expect to continue to see the discovery and development of innovative technologies. As humans develop and harness more powerful biotechnologies, such as CRISPR-cas9, we expect other biotechnologies will become obsolete.

Rivalry Among Existing Competitors (High) - Because successful biotech therapies can be wildly profitable for the companies that own the relevant intellectual property, industry competition is often fierce. For example, let's consider the world's most commercially successful drug, Humira (owned by AbbVie), which had sales of $5.4 billion in the first half of 2022. Many well-funded competitors, such as Amgen and Mylan, have tried to launch sales of their own biosimilar to Humira. AbbVie has aggressively defended its sales of Humira by obtaining many patents and litigating to protect those patents, particularly in the U.S., which is the largest market for most biotech companies. When the key patents for Humira inevitably expire, AbbVie is bound to face a deluge of competition.

In the Biotechnology industry, competition must typically wait for a patent exclusivity period to end. The Biologics Price Competition and Innovation Act (BCPIA) provides new biologics with 12 years of marketing exclusivity, during which rivals may not launch biosimilars. Another form of exclusivity is for orphan drugs. The first sponsor of an orphan drug for a designated rare disease or condition receives seven years of marketing exclusivity. Companies will try to effectively extend the exclusivity period for their drugs as far out as possible by applying for more patents. If the added patents are weak, competitors might contest them.

OTHER COMPETITIVE FACTORS

Biosimilar Competition

Biosimilars can typically be marketed once the original branded drug loses FDA-granted exclusivity and patent protection. The firm that manufactures the original biologic is typically referred to as the innovator. Biosimilar development in the U.S. has been hindered by branded biologic drug manufacturers who use tactics such as patent thickets, rebates, and bundled pricing to exacerbate the costs and challenges of biosimilar manufacturers. Some tactics are much less effective internationally because health care systems outside the U.S. are often more centralized. In addition, since biosimilars are typically slightly different from the original biologic, the FDA has set guidelines that make it expensive and difficult for biosimilar manufacturers to prove that their biosimilars are interchangeable with the innovator's drug. To this day, none of the FDA-approved biosimilars are considered interchangeable, which deters physicians from prescribing them. In Europe, biosimilars are much more readily substituted than in the U.S.

Due to the challenges in the U.S., biosimilars have not affected the biologic drug market as much as initially hoped. Biosimilars have helped lower prices where they are available, but not to the same extent that simple molecule pharmaceuticals face when a generic drug hits the market. Biosimilars are typically priced at about a 30% discount, while generic drugs are typically priced at an 85% discount to the originator's compound. We expect biosimilar discounts to increase over time as biosimilars become more common in the U.S. and the FDA provides a clearer pathway to achieving interchangeability. At the end of 2019, the CREATES Act was signed into law, a small step towards increasing the viability of biosimilars. The CREATES Act prevents branded drug makers from refusing to sell drug samples to biosimilar and generic manufacturers. We expect to see more proposals in the future to support the growth of biosimilars in the U.S.

Biosimilars have significantly reduced medical costs in Europe, as the European Union (EU) had approximately 73 approved biosimilars for 18 reference products as of July 2022, the vast majority of which are marketed. The first EU biosimilar was approved in 2006. Meanwhile, the U.S. approved its first biosimilar in 2015 and has since approved approximately 37 biosimilars for 13 reference products, excluding insulin biosimilars, as of September 2022. Only 22 of the approved biosimilars are marketed in the U.S. because of barriers to entry. Barriers in the U.S. to biosimilars tend to be much more difficult to overcome because the U.S. market is the largest and most important regional market for almost all drug manufacturers.

New Patent Issuances Detract from Biosimilar Cost Savings

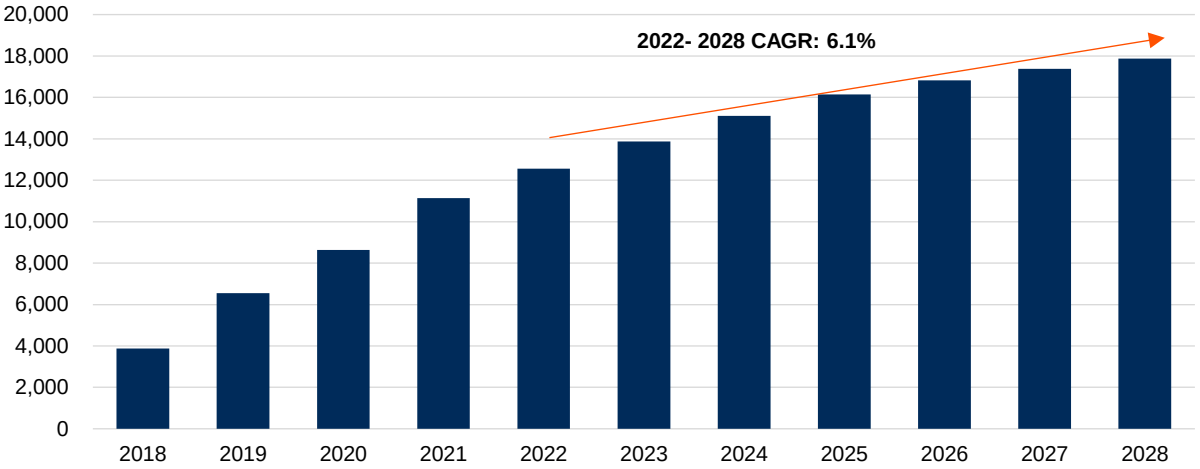
Despite the promise of biosimilars to replace older medicines with cheaper alternatives, several legacy biologic drugs have been issued new patents that extend product lifecycles and are likely to keep biosimilar competition off the market indefinitely.

For example, Biogen's original patent for Avonex (a drug for multiple sclerosis) was set to expire in 2013, but the company was granted a new patent in 2009, which effectively extended patent protection for the drug until 2026. Another example is Humira, a drug that has a composition of matter patent, which expired in December 2016. However, AbbVie (manufacturer of Humira) filed at least 70 other patents related to Humira's formulation and manufacturing, deterring aspiring biosimilar competitors. As a result, the company is not expected to face significant biosimilar competition to Humira in the U.S. until 2023, despite the December 2016 patent expiration.

These extensions make it difficult for biosimilar manufacturers to enter the market.

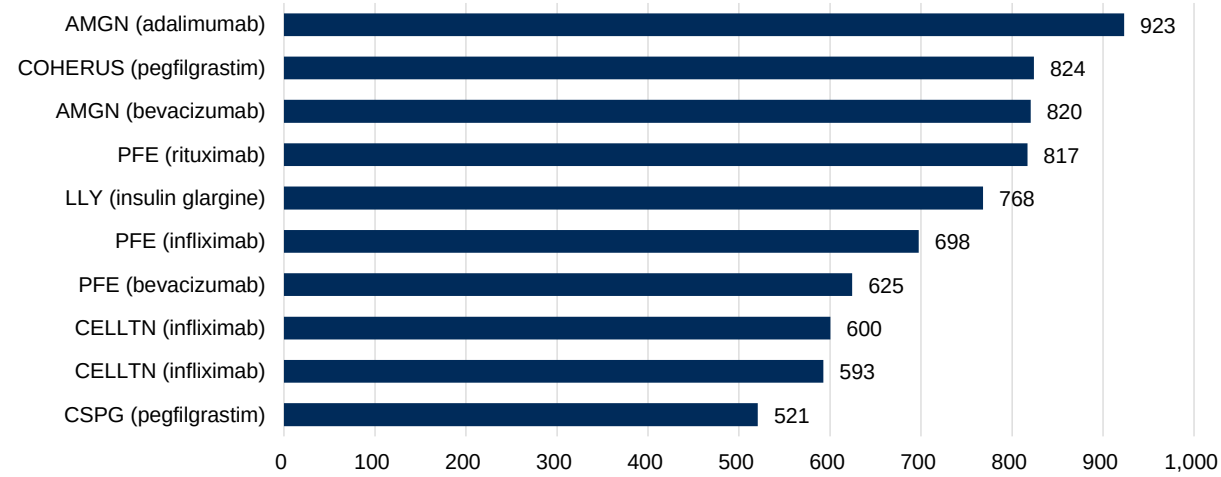
The 2012 introduction of the Inter Partes Review (IPR), a trial proceeding conducted by the Patent Trial and Appeal Board (PTAB) to challenge the validity of a patent, has slowed down the trend of patent extensions. Compared to litigation, the IPR is faster, cheaper, and has a higher chance of success.

WORLDWIDE BIOSIMILARS MARKET OUTLOOK
(in $, billions)



Source: Evaluate.

TOP 10 BIOSIMILARS
(ranked by 2028 forecast global sales, in $, millions)



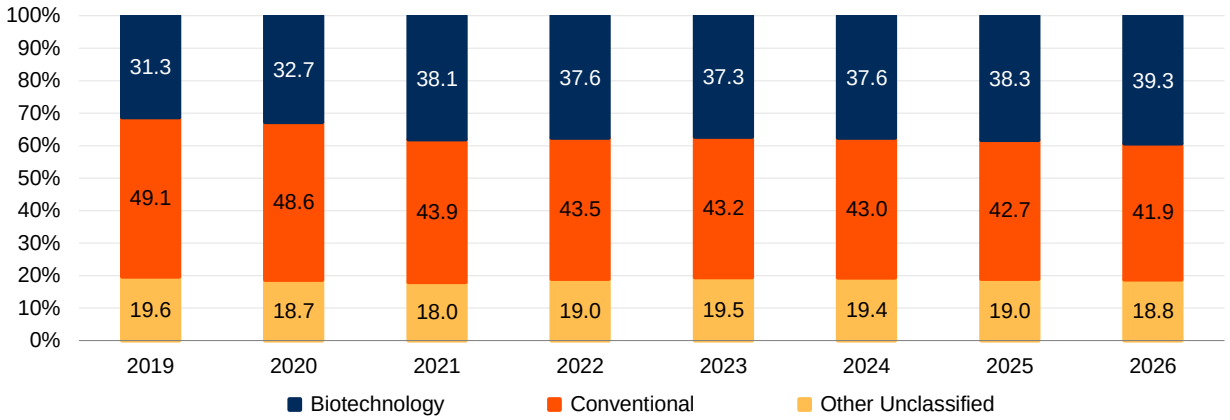
Source: Evaluate.

Operating and Regulatory Environment

Biotech's Presence Grows, Along with Its Ties to Big Pharma

In the last several years, the U.S. Biotechnology industry has experienced a strong pick-up in initial public offerings (IPO), mergers, and acquisitions. Many major pharmaceutical manufacturers have turned their focus to biotechnology. The trend has blurred the distinction between pharma and biotech companies.

GLOBAL SHARE OF PRESCRIPTION DRUG & OTC PHARMA SALES



*Biotechnology refers to modern techniques that use newer applications of biotechnology, such as genetic engineering and cell fusion.
Conventional refers to traditional techniques of using living organisms to yield new products or modify foods for human use.
Source: Evaluate. Data as of September 1, 2022.

Sales from biotech products increased to $418 billion in 2021 from $166 billion in 2012, reflecting a compound annual growth rate (CAGR) of 10.8%. According to data provider Evaluate, 52% of worldwide prescription drug sales from the top 100 products in 2020 (latest available) came from biologics versus 38% in 2012. Evaluate forecasts that this figure will increase to 57% by 2026.

TOP 10 BIOTECHNOLOGY DRUGS
(ranked by year Q2 2022 global sales, in $, millions)

RANK	PRODUCT	COMPANY	MECHANISM OF ACTION	SALES				
				2018	2019	2020	2021	2022*
1	Humira	AbbVie	Tumor necrosis factor alpha (TNFa) antibody	20,476	19,735	20,409	20,694	5,363
2	Keytruda	Merck & Co	Programmed cell death protein 1 (PD1) antibody	7,198	11,121	14,380	17,186	10,061
3	Revlimid	Celgene	Interleukin-6 (IL-6) antagonist; Natural killer (NK) cell stimulant; Natural killer T-cell (NKT) stimulant; Tumor necrosis factor alpha (TNFa) inhibitor; Vascular endothelial growth factor (VEGF) inhibitor	9,816	11,161	12,154	12,821	5,298
4	Eliquis	Bristol-Myers Squibb	Coagulation factor Xa inhibitor	6,438	7,929	9,168	10,762	6,446
5	Eylea	Regeneron	Vascular endothelial growth factor receptor (VEGFR) antagonist	7,164	7,989	7,909	9,385	4,877
6	Stelara	Johnson & Johnson	Interleukin-12 (IL-12) antibody; Interleukin-23 (IL-23) antibody	5,294	6,600	7,707	9,134	4,887
7	Opdivo	Bristol-Myers Squibb	Programmed cell death protein 1 (PD1) antibody	7,524	7,989	7,917	7,523	3,986
8	Biktarvy	Gilead Sciences	HIV-1 integrase inhibitor; HIV-1 nucleoside reverse transcriptase inhibitor (NRTI)	1,184	4,738	7,259	8,624	4,707
9	Xarelto	Johnson & Johnson	Coagulation factor Xa inhibitor	2,477	2,313	2,345	2,438	1,117
10	Imbruvica	AbbVie	Bruton's tyrosine kinase (BTK) inhibitor	4,454	5,686	6,612	5,408	1,145
			Total Top 10	72,025	85,260	95,861	103,975	47,887

*As of Q2 2022.
Source: Company reports, Evaluate.

Inflation Reduction Act 2022 Enacted to Reduce Drug Prices

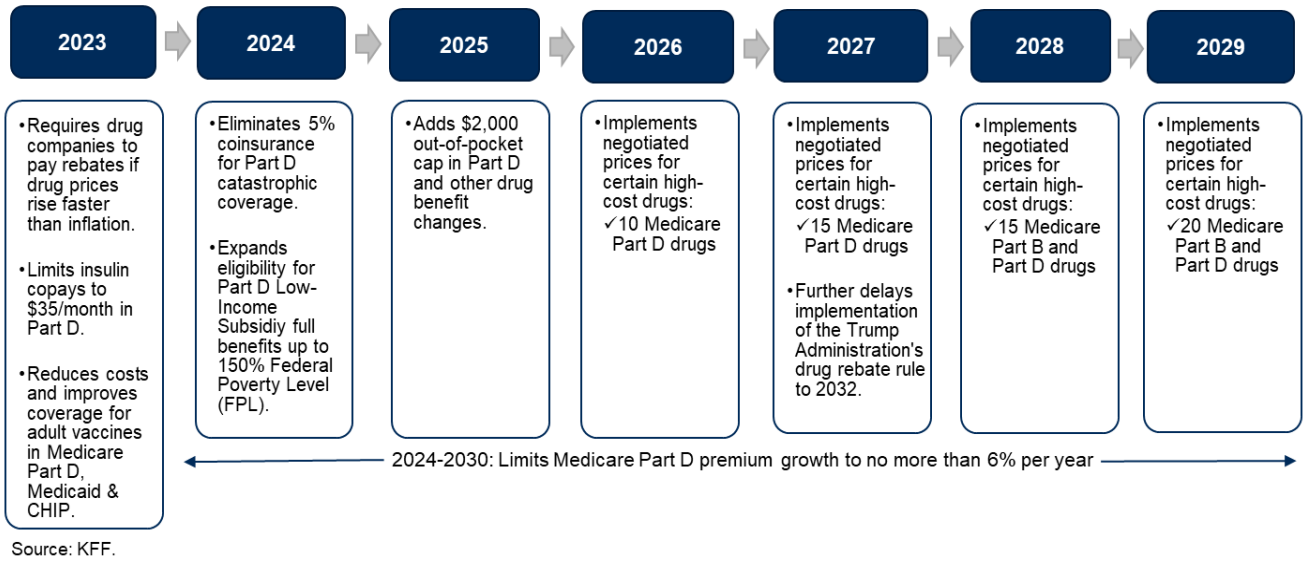
On August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022, which consists of an extensive package of health, tax, and climate change provisions. The law includes some provisions to reduce prescription drug costs for Medicare beneficiaries and lower drug spending by the federal government.

The law also includes two policies that would directly impact overall drug prices. One of the policies requires the federal government to negotiate prices for some high-cost drugs covered under Medicare. This would affect the Medicare Part D and B drug spending, where the spending is highly concentrated among a relatively small share of covered drugs, primarily those without generic or biosimilar competitors. Under the Inflation Reduction Act, negotiation is eligible for brand-name and biologic drugs without generic or biosimilar equivalents covered under Medicare Part D (retail prescription drugs) or Part B (administered by physicians), which are among the highest-spending Medicare-covered drugs. In order to be eligible for negotiation, the drugs should also be nine or more years (small-molecule drugs) or 13 or more years (biologicals) from FDA approval, according to the law. Another policy covered under the Inflation Reduction Act requires drug manufacturers to pay rebates to Medicare if they raise prices faster than inflation for drugs used by Medicare beneficiaries. According to Kaiser Family Foundation (KFF), half of all drugs covered by Medicare saw price hikes above the inflation rate of 1% over the period from 2019 to 2020. On top of that, one-third of these drugs also had price increases of 7.5% or more than the annual inflation rate in early 2022. The inflation rebate provision will be executed in 2020, where 2021 will be used as the base year for establishing price changes relative to inflation.

In addition, the Inflation Reduction Act also includes some provisions that will help to lessen out-of-pocket spending for Medicare beneficiaries. One of the provisions consists of a cap on Medicare beneficiaries' out-of-pocket spending under the Medicare Part D benefit, where coinsurance above the catastrophic threshold will be eliminated in 2024 and a $2,000 cap on spending will be added in 2025. Furthermore, the law also limits cost-sharing for insulin to $35 per month for Medicare beneficiaries starting in 2023, including covered insulin products in Medicare Part D and for insulin furnished though durable medical equipment under Medicare Part B. As of 2023, the law discards cost sharing for adult vaccines covered under Medicare Part D and enhances access to adult vaccines under Medicaid and Children's Health Insurance Program (CHIP). In 2024, the eligibility for full Part D Low-Income Subsidies (LIS) will be expended to low-income beneficiaries, with incomes up to 150% of poverty and modest assets and the partial LIS benefit currently in place for individuals with incomes between 135% and 150% of poverty will also be revoked.

The Inflation Reduction Act also encompasses a provision to further postpone the implementation of the Trump Administration's drug rebate rule until 2023 instead of taking effect in 2027. The rebate rule would eradicate the anti-kickback safe harbor protections for prescription drug rebates negotiated between drug manufacturers and pharmacy benefit managers (PBMs) or health plan sponsors in Medicare Part D.

IMPLEMENTATION TIMELINE OF DRUG PROVISIONS IN THE INFLATION REDUCTION ACT



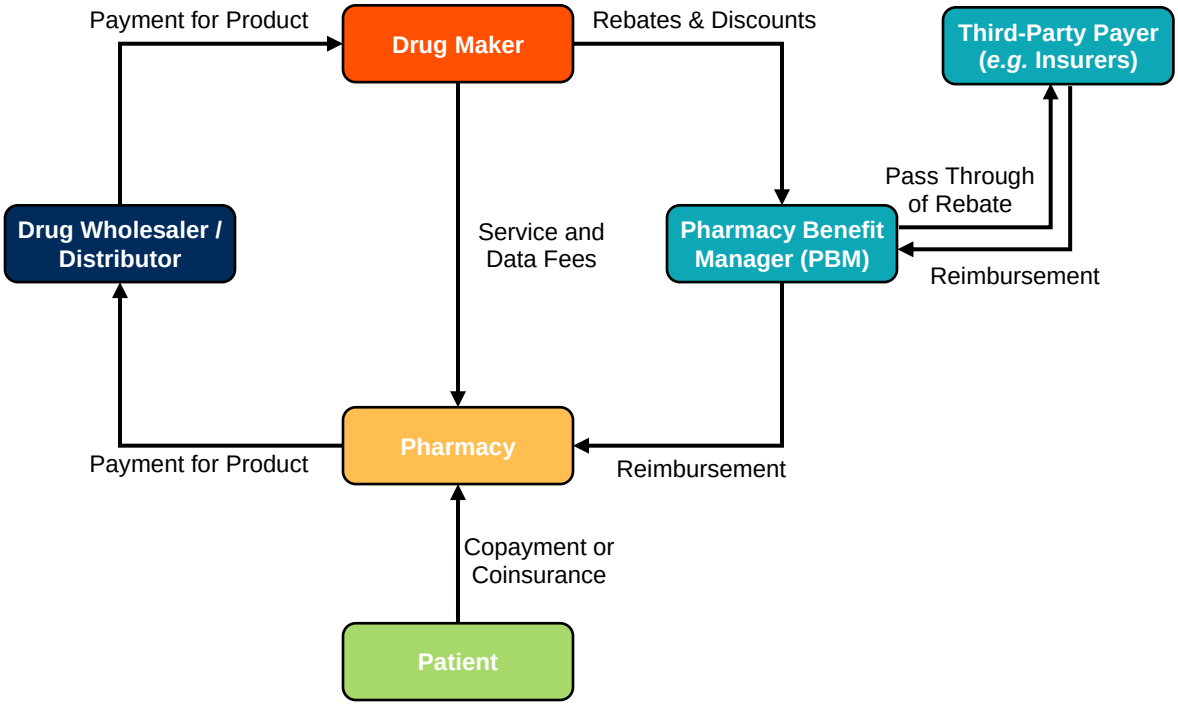
Source: KFF.

Drug Pricing Picture is Complicated and Opaque

Constructive options to address drug prices appear limited because of the opaqueness around the true cost of drugs (*i.e.,* after rebates and discounts) that industry participants deliberately perpetrate. For example, in a study by IQVIA, the average list price of branded drugs grew by 4.4% in 2020 (latest available) compared to 5.2% growth in 2019, whereas the average net price (*i.e.*, the price after discounts and rebates) declined by 2.9% in 2020 compared to 1.7% growth in 2019. In addition, the way that payments flow in the U.S. health care system makes it difficult to point out the key actors or areas of the supply chain that are driving cost trends (see illustration on the next page). Typically, a drug maker sells to a wholesaler, which in turn sells the drugs to a pharmacy, where the patient gets prescription drugs. Other consumer products often go through a similar process; however, in the health care system, the third-party payers (*e.g.*, health insurers and Medicare) negotiate lower prices on behalf of patients (*e.g.*, rebates and discounts) and may provide reimbursements to patients for costs incurred.

The prices that patients pay vary by insurer and health plan. One way that insurers can lower costs for patients is by negotiating rebates with drug manufacturers. Insurers can pass the rebates on to consumers by reducing insurance premiums or drug prices at point of sale; however, it is extremely difficult to determine how various rebates and discounts are being allocated and reflected in health care costs, especially since negotiated savings are not publicly disclosed.

ILLUSTRATIVE FINANCIAL FLOW OF THE U.S. HEALTH CARE SYSTEM*



*This diagram is not meant to be comprehensive or reflective of all financial relations in the industry.
Source: CFRA.

Drug manufacturers have blamed the Pharmacy Benefit Managers (PBMs) for the significant rise in drug prices because of the increased rebates that the PBMs demand. According to Johnson & Johnson, the drugs it sold in 2020 (latest available) had an average list price increase of 3.8%; however, the average net price declined 5.7%. The PBMs, on the other hand, have blamed the drug manufacturers, saying that they need higher rebates and discounts because of the rising list prices of drugs. In August 2018, CVS, one of the largest PBMs in the U.S., commented that it had historically only kept 2% of rebates. The company went a step further in December 2018 with the launch of its "guaranteed net cost" pricing model, which returns 100% of drug rebates to its clients. It seems that rebates may not have been the biggest driver of drug prices, as some believed.

The Covid-19 pandemic highlighted the importance of pharmaceutical innovation and appropriate R&D spending to develop fast and effective cures to diseases. The major argument against lowering drug prices has been the potential negative impact on revenues, which would result in lower research costs and limited future innovation. To counter negative attention over high drug prices, some drug companies have become more vocal. Companies have launched marketing campaigns that focus on the drug industry's substantial R&D spending and the many medical advancements that have been made. Due to the necessity to find a balance between more affordable drug prices and not harm innovation, there are disagreements about specific policy actions to be taken and their implementation. In our opinion, it may take some time to resolve these issues.

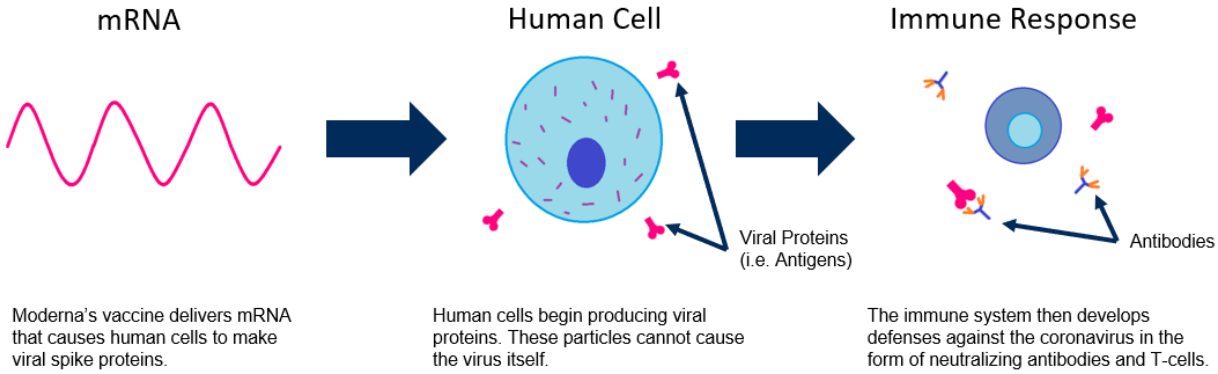
The Pandemic was a Breakout Moment for mRNA-based Therapies

At the beginning of the pandemic, Moderna, a leading developer of mRNA-based therapies, had no commercialized products and was widely expected to be earnings negative through 2022. In addition, no

mRNA-based vaccine had ever been approved before by the FDA. Now, the leading Covid-19 vaccines are both mRNA-based, and Moderna's vaccine net sales was over $17 billion in 2021.

We think that mRNA-based therapeutics are primed to revolutionize the biopharmaceutical industry. mRNA is critical to the body's production of all proteins required for life because mRNA carries the instructions for protein production. Another way to think of mRNA is as software code that tells your body what types of proteins to produce. In the graphic below, we illustrate how Moderna's vaccine works. A key benefit to mRNA therapies over most commercially available biotechnology-based therapies is that mRNA therapies use the recipient's body to produce the desired proteins, whereas many of the most commercially successful therapies are based on proteins that are synthesized outside of the human body. In addition, the manufacturing process for conventional vaccines, in particular, is typically complex and lengthy because such vaccines are made from finicky cell cultures that must grow in a certain way. mRNA therapies promise to significantly reduce production costs and time since the process for manufacturing mRNA vaccines is cell-free. In our opinion, mRNA therapies could become the next big driver of value creation for the biopharmaceutical industry.

How Moderna's mRNA-based Vaccine Works



BioNTech, a biotechnology company headquartered in the German city of Mainz, made its mark by developing Covid-19 vaccines with Pfizer. BioNTech, which is a cancer company, was able to shift its focus from fighting cancer to creating a Covid-19 vaccine. The company's significant achievement in developing the Comirnaty vaccine managed to save millions of lives and, at the same time, contribute unprecedented windfall of cash to the company. It has managed to earn a total amount of €19 billion in cash, a part of its assets, which equates to "a lifetime of funding" from the vaccine development. As a result, the company aims to resume pursuing its plan in oncology, with ambition to be able to tailor drugs to each patient's cancer.

According to *Financial Times*, the company utilized the messengerRNA (mRNA) technology in the development of Covid-19 vaccine and targets to use the same technology to tackle cancer in combination with other therapies. The company also believes that the consolidation of various treatments, including cell therapies, antibodies, and other ways of modulating the immune system, would be the best hope of developing a cure for cancer. In April 2022, it revealed the results of a study that combined mRNA with CAR T-cell therapy to reprogramme a patient's immune system. CAR T is a complex treatment that involves collecting and modifying a patient's immune cells to fight their cancer and has so far only worked in blood cancers. However, BioNTech scientists went the extra mile in developing an mRNA booster with the intention to make it useful in a larger range of cancers. The study also disclosed that the booster managed to expand the number of immune cells and boost their capability to eradicate a solid tumor.

In addition, the company's most advanced clinical oncology program is for cancer vaccines. As opposed to regular vaccines, they do not prevent the recipient from developing cancer, but are used as treatments to

alert the immune system to kill mutated cells. Even though the cancer vaccines concept has been around for decades, it has unfortunately been a non-success. Experts think that the failure could be attributed to the delay of therapies deployment, where new therapies are typically attempted in patients who have not responded to previous drugs and are normally at the later stage of cancer. However, experts believe that cancer vaccines might have the potential to work better at an earlier stage of cancer when the patient's immune system is more vigorous. BioNTech countered the experts' claim and emphasized that its early data suggested that its mRNA cancer vaccines are evoking immune responses several hundred times stronger than were previously reported for conventional cancer vaccines. On top of that, the company is also performing trials in earlier stage cancers and intends to provide the vaccines shortly after patients' surgery to remove the primary tumor has been completed. In a phase 1 trial conducted in June 2021, the company saw positive results in treating pancreatic cancer patients momentarily after surgery.

Nonetheless, BioNTech foresees challenges in convincing "conservative" regulators to adapt to individualized therapies that break the mold of conventional clinical trials. Although these challenges, coupled with scientific success uncertainty, could create a long journey ahead for the company, its latest scientific discoveries and implementation of advanced technologies could give new hope to cancer patients.

Specialty Drugs Outpace Inflation

Specialty drugs—which are often biologics—are a recent designation for therapeutics that are considered high-cost, high complexity, or high touch. The cost of specialty drugs is increasing at a far higher rate than inflation. Evernorth, a pharmacy benefit management firm, predicts that specialty drug spending will potentially increase by 10%-15% within the next few years. As of March 2022, specialty drugs accounted for 55% of total drug spending, driven by growth in autoimmune, oncology, and diabetes, according to IQVIA.

In 2020, list prices for specialty brand medications climbed 36% from 2016, based on Evernorth Prescription Price Index for 2020 (latest available). In contrast, prices of specialty generic medications plummeted 42.3% in the same period. It is hard to tell how the price of brand-name drugs has changed for end consumers because of all the rebates and discounts used in the industry.

HOW THE INDUSTRY OPERATES

Biotech refers to the application of biological and biochemical sciences in the large-scale production of products to change human health, food supplies, or the environment.

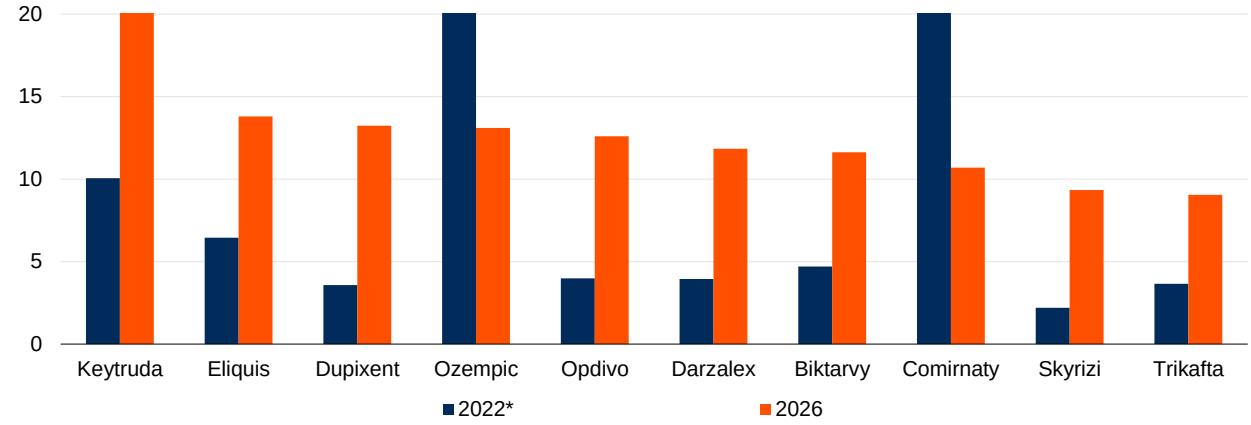
Key Biotechnologies

Monoclonal antibodies (mAb) have been and continue to be a key industry driver, as mAbs are used in many leading drugs for the treatment of cancer and inflammatory disease. Leading mAbs for inflammatory diseases include Johnson & Johnson's Remicade, AbbVie's Humira, and Roche's Avastin. Evaluate estimates that four of the top 10 best-selling biotechnology products in 2026 will be based on mAb technology.

Other biotechnologies that we expect to be marketed in the future include cell therapies, gene therapies, recombinant products, and bioengineered vaccines. There are even newer technologies being considered for commercial development, such as CRISPR/Cas9 (a type of gene therapy). We could see significant changes in the landscape of the biotechnology market as new technologies gain prominence.

TOP 10 SELLING DRUGS WORLDWIDE IN 2026*

(in $, billions)



*As of Q2 2022.

Source: Evaluate.

Spending on R&D

Investment in research & development (R&D) is crucial to building a long-term sustainable organization. Biotech R&D as a percentage of product sales has traditionally been high, but it has declined as industry revenues have expanded substantially. While declines in R&D spending can negatively affect investor sentiment because of R&D's role in innovation, R&D spending for the whole industry has been increasing. Successful drug companies are those, in CFRA's view, that can manage and develop robust pipelines and combine them with commercial success. Peak drug sales typically occur five to seven years following the launch of a new drug.

RESEARCH & DEVELOPMENT EXPENDITURES FOR U.S. BIOTECHNOLOGY COMPANIES*
(arranged by Q2 2022 R&D expenditures)

COMPANY	R&D EXPENDITURES ($ mil)						R&D / REVENUES (percent)					
	2017	2018	2019	2020	2021	2022**	2017	2018	2019	2020	2021	2022**
Gilead Sciences	3,734	5,018	9,106	10,895	5,540	1,432	14%	23%	41%	44%	20%	23%
AbbVie	5,334	10,753	6,792	7,755	8,046	1,878	19%	33%	20%	17%	14%	13%
Amgen	3,562	3,737	4,116	4,207	6,324	1,039	16%	16%	18%	17%	24%	16%
Biogen	2,374	2,710	2,281	4,066	2,519	529	19%	20%	16%	30%	23%	20%
Regeneron Pharmaceuticals	2,075	1,469	2,450	2,735	2,908	877	35%	22%	31%	32%	18%	31%
Incyte	1,329	1,198	1,154	2,224	1,488	371	87%	64%	53%	83%	50%	41%
Vertex Pharmaceuticals	1,580	1,445	1,755	1,830	3,051	662	63%	47%	42%	29%	40%	30%
Exelixis	112	182	337	548	694	199	25%	21%	35%	55%	48%	48%
United Therapeutics	265	358	1,183	358	540	94	15%	22%	82%	24%	32%	20%
Emergent BioSolutions	97	143	226	235	234	50	17%	18%	20%	15%	13%	21%
Xencor	72	98	119	170	193	47	201%	240%	76%	138%	70%	156%
REGENXBIO	57	84	124	166	181	61	551%	38%	352%	108%	39%	187%
Coherus BioSciences#	167	110	94	143	363	42	10706%	N/A	26%	30%	111%	69%
Arrowhead Pharmaceuticals	51	58	87	142	236	72	167%	122%	53%	178%	163%	223%
Enanta Pharmaceuticals	63	112	140	141	186	39	48%	47%	75%	138%	200%	201%
Cytokinetics	90	89	86	97	160	57	675%	283%	321%	174%	227%	64%
Myriad Genetics	71	80	83	73	82	20	9%	10%	10%	13%	12%	11%
Ligand Pharmaceuticals	27	28	56	59	69	19	19%	11%	46%	32%	25%	33%
Vanda Pharmaceuticals	39	44	49	56	75	21	23%	23%	21%	22%	28%	33%
Halozyme Therapeutics	151	150	141	34	36	15	48%	99%	72%	13%	8%	10%
Eagle Pharmaceuticals	33	44	37	31	51	11	14%	21%	19%	16%	30%	15%
Anika Therapeutics	19	18	17	26	28	7	17%	17%	15%	20%	19%	18%
Spectrum Pharmaceuticals§	52	75	79	109	87	0	40%	69%	N/A	N/A	N/A	N/A
Average	928	1,217	1,327	1,570	1,439	328	558%	58%	66%	56%	55%	58%
Median	97	112	140	166	234	57	25%	23%	38%	30%	29%	30%

*Based on companies in the S&P Composite 1500 Biotechnology Index.

**As of Q2 2022.

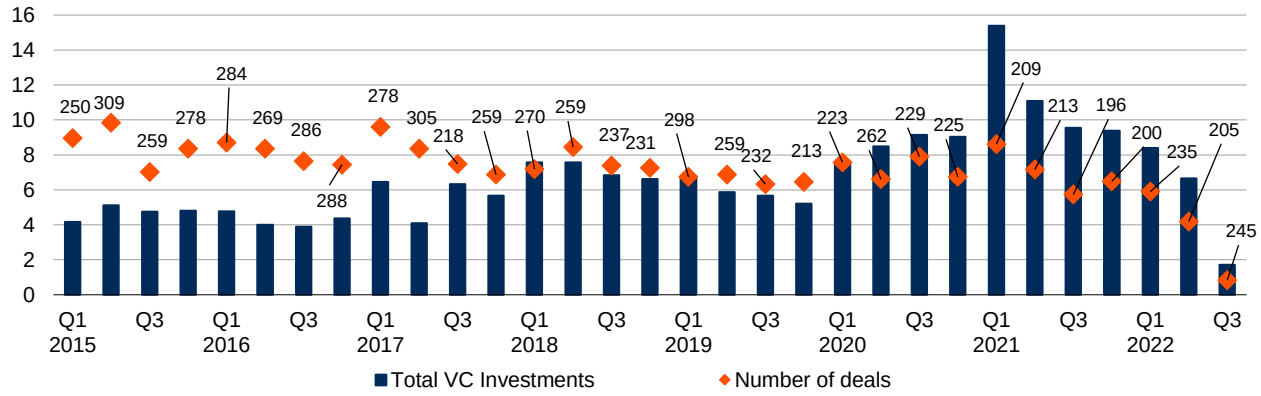
#No revenue in 2018. §No revenue in 2019 and 2020.

Source: CFRA, S&P Global Market Intelligence.

Access to Capital is Crucial

Given the high costs of biologic R&D, access to capital is critical for biotechnology companies, particularly for those that have not had significant commercial success. New biotech entities are usually funded through seed money from wealthy private investors or small groups of investors, called “angels,” and by venture capitalists. In market downturns, funding can become especially scarce, which can derail R&D plans. CFRA recommends reviewing the access to funding, cash flow, and cash and cash equivalent balances for biotechnology companies to assess the capacity for a company to continue funding its clinical pipeline. This is especially pertinent for young biotech firms that may not have had much commercial success yet.

GLOBAL QUARTERLY BIOPHARMA VENTURE INVESTMENTS*
($, billions)



*Data as of September 1, 2022, includes MedTech investments.
Source: Evaluate.

The Importance of Partnerships

Once a small firm has a promising investigational drug candidate, the firm often chooses to team up with a major pharmaceutical or biotech company. The larger company may supply upfront fees, R&D funding, milestone payments, royalties, and co-promotion rights. In addition, the partner often supplies regulatory know-how, production facilities, and sales organizations for new products. It usually makes sense for small companies to license their initial products or collaborate with big players since it is difficult to navigate regulatory and commercial payor landscapes. In addition, establishing support within a physician community often requires significant effort and cost. Eventually, small companies gain enough experience, scale, and financial support to hopefully commercialize their own products.

Many approved biotech products have been developed through collaborative agreements. Such agreements have become a hallmark of the biotechnology and pharmaceutical industries. These agreements have often led to acquisitions between partnering firms after the larger firms gain first-hand insights into a smaller company’s management, breadth of research capabilities, and prospects for pipeline advancement.

These agreements aren’t only beneficial to small companies. Large companies benefit because they can often acquire the rights to innovative assets with a high chance of commercial success. This saves time a lot of time and R&D costs. In addition, large companies usually already have well-established sales and marketing infrastructure that they can leverage to sell new drugs similar to the ones they already sell.

Patents Make It Happen

Patents are among the most important benchmarks of progress in developing new biotechnology products. When a company obtains a patent for a new process or product, competitors are prohibited from the commercial use of that discovery. In the Biotechnology industry, patents are critical to raising capital for continued R&D spending. Patents granted by the U.S. Patent and Trademark Office (USPTO) can be challenged via either the Inter Partes Review (IPR) or through court proceedings. IPRs tend to be faster, cheaper, and more successful.

Nevertheless, there have been several ongoing patents feud between the biopharmaceutical companies in the industry. One of the ongoing feuds involves the “skinny label” patent battle between Teva Pharmaceuticals and Glaxo Smith Kline (GSK). In 2007, Teva launched its Coreg generic in two of the branded med’s three indications and the FDA later instructed the company to add the med’s third indication for congestive heart failure in 2011, although GSK owned a patent for that particular use through 2015. In light of this, GSK filed a lawsuit in 2014 claiming that Teva prompted doctors to prescribe its copycat for congestive heart failure, while Teva countered that it was merely acting as per the FDA’s instructions. In 2017, a jury sided with GSK and ordered Teva to pay $235 million, which Teva later induced a district court to overturn the verdict. However, an appeals court reversed the ruling and reinstated the original finding of infringement including $235 million in damages. In February 2022, Teva requested for the U.S. Court of Appeals for the Federal Circuit to rehear its case, but its request was denied. Nonetheless, in July 2022, Teva once again urged the U.S. Supreme Court to consider overturning its $235 million loss in the patent feud. The company argues that this litigation could substantially impact the common practice among generic drug makers and could potentially cause “competition-killing uncertainty” that would hurt the U.S. health care system.

On the other hand, Gilead and Bristol-Myers Squibb have been rivals in developing drugs for CAR T-cell therapy in the industry. In April 2022, Gilead made its mark when Yescarta became the first drug to receive FDA approval for CAR T-cell therapy for initial treatment of relapsed or refractory Large B-cell Lymphoma (LBCL). Bristol-Myers Squibb merged as a contender when the FDA gave the nod on Breyanzi for CAR T-cell therapy with broader approval shortly after in June 2022. Gilead’s Yescarta is intended for LBCL patients who are refractory to one prior therapy or who relapse within 12 months of first-line chemoimmunotherapy. On the other hand, Bristol Myers Squibb’s Breyanzi covers the same patient population but includes a specific line about patients who are not eligible for stem cell transplants, an untapped population by Yescarta.

On August 26, 2022, another patent feud emerged between Moderna and Pfizer, where Moderna sued Pfizer for infringement of three of its patents associated with messenger RNA, the fundamental genetic material of their vaccines. Moderna asserts that its patents may cover technology that could also be imperative to future vaccines, where it could leverage on potential licensing of its innovations to pharmaceutical companies attempting other medical breakthroughs. We think that the companies involved in the development of Covid-19 vaccines may encounter more lawsuits in the near future, as the mRNA technology becomes more renowned in the biotechnology industry.

Clinical Trials: Putting Candidates to the Test

The U.S. drug approval system is one of the world’s most stringent. Biotechnology medications undergo the same lengthy testing process as any other pharmaceutical product to prove safety and efficacy.

The clinical testing period in humans usually consists of three phases. During Phase I, the drug is administered to a small number of healthy people to test its safety in small doses. If this initial test appears successful, the dosage is slowly increased to determine its safety at higher levels. During Phase II, the drug is given to patients suffering from the disease or a condition that the drug is intended to treat. This round of tests is designed to evaluate the drug’s effectiveness and safety, and generally includes a larger patient population and a lengthier test period than Phase I. Determining a drug’s efficacy earlier in the

clinical process can boost R&D productivity and allow companies to fail faster and devote resources to the most promising candidates.

Drugs that pass these hurdles then undergo Phase III, in which the most complex and rigorous tests are performed on large groups of ill patients to verify the drug's safety, effectiveness, and optimum dosage regimens. Physicians closely monitor patients to determine efficacy and identify adverse reactions. Usually, Phase III trials employ randomized, double blind tests with placebo control to remove any chance for bias. This means that one group of patients is given the drug, and another is given an inert substance (*i.e.*, a placebo); however, if there is already an approved drug for the indicated use, it will be used instead of the placebo. Neither the patients nor their doctors are aware of which patients are receiving which drug.

After the development work is complete, company scientists analyze the data. If the data are positive, the company compiles it into a biologics license application (BLA) or a new drug application (NDA), which is submitted to the FDA for review. The application has results of the preclinical and clinical research, and includes details of the product's formula, production, labeling, and intended use. According to Evaluate, approximately 68% of drugs make it from Phase I to Phase II, 33% from Phase II to Phase III, 55% make it from Phase III to Filed, and 93% make it from Filed to Approved status. Overall, 11% of drugs make it from Phase I to approval. The FDA approval is a rigorous process; out of 5,000 compounds discovered in the preclinical stage, only about five will make it through the entire approval process. Because drug manufacturers often endure losses related to failed drug candidates, they try hard to maximize and protect the profits of the drugs that do find commercial success.

Regulatory Filing and Review

The FDA's Center for Drug Evaluation and Research (CDER) reviews therapeutic biological products and chemical-based drugs. The Center for Biologics Evaluation and Research (CBER) reviews blood products, vaccines, and tissue-based products.

BLAs and NDAs are typically voluminous documents, sometimes exceeding 100,000 pages. Once an NDA or BLA is approved, the FDA determines the drug's official labeling, including a detailed description of the drug and its composition, indicated uses (also called indications), contraindications, and side effects. This information is included in a drug's package insert.

Following approvals, the FDA continues to monitor drugs because side effects or other unexpected developments may arise or become known. The FDA may require additional post-market studies (Phase IV) to evaluate long-term effects. Such studies are becoming more common. Often, after marketing has begun, the manufacturer sends supplemental applications to request approval to use a drug for added indications. For the initial application, manufacturers tend to seek narrow indications that target a well-defined set of patients. Added approvals can expand the market size and commercial potential of a biologic.

Shortage of Clinical Trial Candidates Slows Industry Pipeline

As of September 6, 2022, the number of registered clinical studies totaled 426,942, according to the NIH. Because of the high number of studies, we have reason to believe that drug makers are finding it increasingly difficult to recruit enough patients to take part in clinical studies, resulting in frequent clinical trial delays. These delays are also caused by increasing demands to show the efficacy of new drugs over existing treatments. Competitive drug therapies often require larger and more expensive studies to show statistically meaningful results.

Expedited Processes for Drugs that Treat Serious Diseases

The FDA has several pathways in place to enable quicker access to treatments for serious diseases, especially for treatments targeting diseases with an unmet need or treatments that have significant advantages over existing ones. The main pathways for expedited approval include priority review,

breakthrough therapy, accelerated approval, and fast track. Use of these designations has had a significant effect on rapidly increasing access to drugs treating conditions such as AIDS and cancer.

A priority review designation means that the FDA aims to take action on the application within six months. The breakthrough therapy designation is meant to expedite the development and review of drugs that may demonstrate a substantial improvement over available therapy. Accelerated approval is geared towards drugs for serious conditions that fill an unmet medical need. Fast track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions that fill an unmet medical need. Drugs that receive the fast-track designation are eligible for the accelerated approval and priority review pathways if the relevant criteria are met.

Examples of approvals granted under the accelerated approval program include Pomalyst and Kyprolis, by Celgene and Amgen, respectively. These were approved ahead of their action dates based on completed Phase II studies. However, accelerated approval does not always result in the eventual grant of full approval.

In rare cases, drugs can be made available before marketing approval is granted through the FDA's investigational new drug (IND) policy for treatments, which allows manufacturers to sell drugs for serious or immediately life-threatening conditions while final clinical work is conducted, and FDA review takes place.

Also, during the pandemic, most Covid-19 therapeutics used the Emergency Use Authorization (EUA) pathway to reach patients. Under the EUA pathway, the FDA may authorize unapproved medical products or unapproved uses of approved medical products for emergency purposes. Products approved under EUA must go through typical approval routes if they are to be sold during non-emergency conditions.

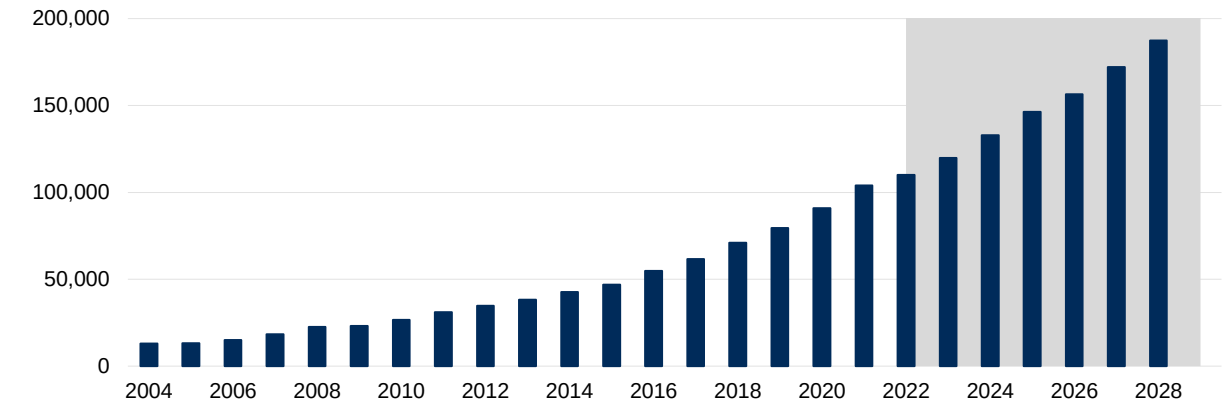
Orphan Drugs

Enacted in 1983, the Orphan Drug Act (ODA) was designed to encourage companies to develop drugs to treat rare diseases afflicting fewer than 200,000 Americans by providing research grants, tax breaks, and seven years of exclusive marketing rights to manufacturers of drugs aimed at patient markets that would otherwise be too small to justify commercial development. As a result, orphan drugs have become more profitable, and development of such drugs has become more prevalent. Data provider Evaluate forecasts an increased presence of pharmaceutical companies in rare diseases.

Orphan drugs have been a key growth driver for the biotechnology industry despite the small patient populations that are targeted. In fact, according to an estimate by Evaluate, worldwide prescription orphan drug sales experienced a CAGR of 13.7% during the 2012-2021 period and are projected to increase at a CAGR of 9.2% from 2022 to 2026.

In the U.S., an estimated 25 to 30 million Americans are living with at least one type of the 7,000 rare conditions identified by the NIH. Because orphan drugs have market exclusivity and typically target life-threatening or debilitating diseases or conditions, drug developers are often able to demand high prices from third-party payers. We think that the average cost could continue rising, especially if companies increasingly manufacture curative therapies. In 2019, the FDA approved the first therapy to cost more than $1 million. Zolgensma, a therapy that alters the underlying genetic cause of spinal muscular atrophy (SMA), launched with a list price of slightly more than $2 million.

ORPHAN DRUGS: WORLDWIDE PRESCRIPTION SALES
($, millions)



Note: Shaded region denotes estimated figures.
Source: Evaluate.

Pricing Considerations

FDA-approved treatments for hard-to-treat, potentially fatal diseases have significant pricing power unless there is substantial competition for such indications. Breakthrough therapies for life-threatening conditions are usually priced exceptionally high as the value of these treatments is bolstered by the high value that American society places on human life. Biotechnology companies often focus their R&D efforts on rare and undertreated diseases. As such, new biopharmaceuticals are typically lucrative, and manufacturers have had wide discretion in pricing them. Many factors go into the pricing decision, such as the relative efficacy of a given drug versus its rivals, the size of the target market(s), the price of competing therapeutics, and costs incurred in development.

The successful commercialization of a drug is based, in part, on the availability of third-party payer reimbursement, including private health insurers and government payers. Private third-party payers, such as health insurers and prescription benefit managers, have increasingly exerted their influence on drug prices by often demanding discounts and rebates to listed drug prices.

CRISPR Gene Editing Potentially Reshaping Cancer Research

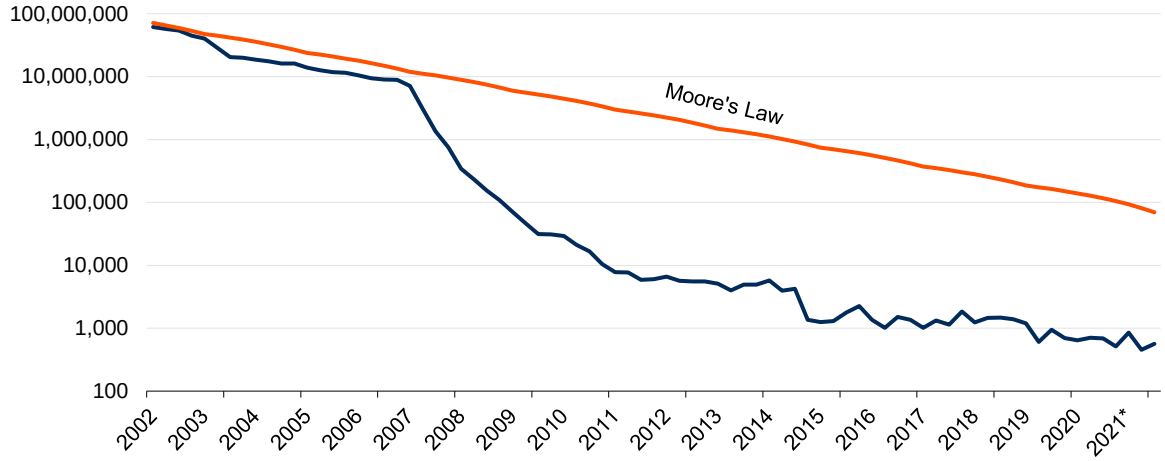
CRISPR or Clustered Regularly Interspaced Short Palindromic Repeats is a gene-editing technique that scientists believe can lead to many medical breakthroughs. In theory, CRISPR, used in conjunction with a CRISPR enzyme, usually Cas9 or Cpf1, allows scientists to cut, edit, and replace DNA sequences to change gene function easily and quickly. The modification could correct genetic defects to treat and potentially cure a wide range of diseases, including cancer. Many innovators working on CRISPR editing tools are small biotech firms, such as Editas Medicine, Intellia Therapeutics, and Crispr Therapeutics. Several larger biotech companies have shown interest by entering into partnerships and collaborative agreements to develop CRISPR-based therapies.

In late 2018, a few firms received regulatory approval to begin human clinical trials in the U.S. and Europe. Although U.S. scientists helped develop CRISPR-Cas9 back in 2012, human clinical trials have generally been prohibited in the U.S. and Europe due to safety and ethical concerns. Some safety issues concern the potential of unintended and irreversible changes to a genome. There are also ethical concerns surrounding gene-editing for non-therapeutic purposes, such as choosing hair or eye colors, etc. In the second half of 2019, several companies began testing CRISPR gene editing on patients, such as CRISPR Therapeutics in collaboration with Vertex Pharmaceuticals and Allergan in collaboration with Editas Medicine.

China has taken a leading role in CRISPR development involving human clinical trials. Since 2016, researchers in China have started human clinical trials with CRISPR modified genes to treat various diseases and cancers, including lung, liver, throat, stomach, head, and neck cancer, among others. Despite many human trials in China, including one that caused a global outcry when a researcher gene-edited a pair of twin baby girls when they were just embryos, not much is known about them. Several patients have died after being treated with a CRISPR therapeutic, but researchers believe the deaths were related to their diseases and not the treatment.

Much of the advancement in gene-therapy and gene-editing technology can be attributed to the significant decline in the cost of genomic sequencing, allowing for the discovery and analysis of genetic variations. In late 2017, the FDA approved the first gene-therapy drug. We expect the cost of genetic sequencing will continue to decline, leading more researchers and companies to explore this field, and potentially accelerate the discovery of new treatments. The cost of genetic sequencing has been on a declining trend since the 2000s. The cost back then for one genome was around $62 million (circa 2002), which compares to a cost of less than $1,000 in 2021.

COST PER GENOME



*Latest available data through August.
Source: National Human Genome Research Institute.

CFRA expects funding and financing for the development of innovative technologies such as CRISPR Therapeutics to accelerate. In early 2018, the NIH, the largest biomedical agency in the world, launched an initiative seeking to remove the barriers that have slowed the adoption of CRISPR technology in treating patients. The NIH launched the Somatic Cell Genome Editing program, which will provide research grants, totaling $190 million over six years, to researchers to improve the delivery mechanism for targeting gene editing tools in patients, develop new and improved genome editors, and develop assays for testing the safety and efficacy of gene editing tools.

The goal of this program is to accelerate the development of CRISPR technologies for the development of therapies to treat genetic diseases. Somatic cells are non-reproductive cells of the body and do not pass DNA down to the next generation. By focusing on somatic cells, any changes to the DNA through gene-editing therapeutics will not be inherited. NIH-funded research has led to many innovative therapies over the past several decades. We forecast this initiative could also lead to the development of new therapies.

The NIH has shown continuous support for research that could potentially help the public. In February 2022, the agency awarded a research grant to the University of Rochester for in-depth investigation of phenotypic plasticity. The study examines organisms' evolutionary survival strategy focusing on their ability to change traits in response to their environment. This research also aims to evaluate traits development

from the integration between environmental and genetic signals, which could potentially contribute to fundamental findings to reduce prevalence of human diseases. The award, which is distributed over five years, will enable further research on the implication of plasticity on human health and disease.

HOW TO ANALYZE A COMPANY IN THIS INDUSTRY

The analysis of a biotech firm involves a thorough study of both business strategy and financial health. Many biotech firms do not have commercial track records, which makes these companies difficult to analyze. Thus, investors sometimes must rely more heavily on qualitative rather than quantitative methods of valuation.

RESEARCHING THE BUSINESS

The first step is to examine a given company's business strategy, core competencies, and market position. Many biotech companies are still in a development phase, so this analysis may rely heavily on qualitative judgments about management skill, technology, and new product potential.

Products and Pipeline

A biotech firm's product portfolio and clinical pipeline are essential to its success. A company's intrinsic value should be primarily a function of the prospective earnings to be gained from approved products and investigational compounds in development, as well as the probability of successfully developing pipeline candidates.

CFRA thinks that companies with technologies that are scientifically sound and patentable, especially those with the potential to lead to additional developments and applications, generally offer better risk-reward profiles than companies that are developing drugs in competitive therapeutic areas.

Companies with multiple drug candidates in late stages of clinical development tend to be more valuable. At the same time, be wary of companies trying to develop many marginally beneficial products (referred to as "me-too" products) in disease areas that are already well served. Such companies may have limited commercial potential.

Patent Protection

In assessing a biotech company's product portfolio, it is imperative to determine the strength and duration of a company's patents on its proprietary drugs and compounds. The loss of market exclusivity on key products can lead to sales erosion from biosimilars. This concern is particularly grave for markets outside of the U.S., where biotech firms typically have fewer ways to protect their intellectual property once they lose exclusivity. The issue of patent protection is poised to become a larger issue in the coming years, as continued progress toward a smoother regulatory pathway for generic biotech drugs takes shape and concerns of high drug prices fuel political rhetoric.

In the U.S., biotech firms often create a patent thicket—a layer of numerous patents that protect the exclusivity of a drug—to make it more difficult for competitors to enter the market, even after a drug's initial patents have expired. Competitors are deterred from competing with drugs with substantial patent thickets because the legal costs would be considerable.

Current patents can lead to royalties if a company decides to license its technology to other firms.

Assessing R&D

Most leading biotech companies spend between 15% and 25% of operating revenues on R&D, with most development-stage biotech companies often spending well over 100%. However, success rates—in terms of developing lucrative new drugs and therapeutics—can differ markedly.

The bigger, better-funded firms tend to have the advantage of being able to hire top scientists and conduct the large, costly clinical trials that are often needed to develop new drugs. Furthermore, in a health care market dominated by managed care (such as the U.S.), a key factor in future success will be a company's ability to develop cost-effective new drugs that constitute therapeutic breakthroughs. New products that supply comparable results to existing therapies are unlikely to achieve great commercial success.

Look for companies that are developing drugs for illnesses that are not adequately served by current treatments. Drugs for chronic illnesses that have large patient populations can provide a higher return on R&D expenditures than one-time treatments, such as vaccines.

Management Strength

The quality and experience of a company's management and scientific teams are critical to long-term success. The industry changes rapidly, so it is crucial for a firm to be led by insightful and quick-thinking individuals who can adapt to volatile circumstances.

Ideally, a biotech company should employ executives who have previously helped develop and commercialize pharmaceutical products. Look for a demonstrated ability to reach milestones. Management should be credible in terms of historically meeting stated goals and key development milestones. Be wary of a company that consistently misses its own targets. CFRA appreciates management teams that have operating experience. It is important that the people running the company thoroughly understand and appreciate how expensive and elaborate the drug development process is.

Making the Most of Alliances

Biotech firms often enter into collaborations and partnerships with other firms. Because of the excessive costs of drug development, a significant discovery made by a small biotechnology company may go nowhere unless the firm can find a well-financed partner to fund clinical trials and help commercialize the product. It is important for biotech firms to choose corporate partners that are committed to seeing the product through to commercialization. Large pharma and biotech companies often have areas of focus, where they have significant research experience and an established sales infrastructure.

Deal terms represent the value that the bigger partner places on a budding biotech company's technology. From the junior partner's perspective, a good deal typically includes a sizable upfront fee from the bigger firm, and may include equity, R&D funding for product development, milestone payments for achieving R&D benchmarks, co-promotion rights, and royalties on sales. Co-promotion rights are usually preferable to royalties. Although, if a junior partner has limited resources, upfront payments may be more desirable than payments tied to future R&D benchmarks.

Many biotech companies maintain both formal and informal relationships with scientists at leading medical schools, research institutions, or government organizations, such as the federal government's NIH. Such relationships can be a valuable resource. Companies with connections to the NIH often gain rights to medications or drug targets discovered by the NIH (usually in conjunction with a leading university).

Financial Resources

Is the company well-financed? A biotech firm must have adequate funding for its development programs, or it may be forced to curtail its R&D efforts. CFRA likes to see enough cash on the balance sheet to cover operating expenses for at least two years. Such a position can safeguard a firm from becoming desperate for funding and thus being forced to accept sub-optimal value on its assets.

An ample cash balance provides a firm with stronger negotiation power when it comes to collaborative arrangements and the ability to continue product development with limited added funding. The farther along a product is in the development process, the greater the potential future profits the firm should be able to keep in any negotiated deal. Having enough cash on hand is also important because access to financing tends to change over time. The biotech industry goes through periods when public equity markets are not particularly receptive to funding risky ventures, and it is important for a company to have enough resources to see it through such times.

Regulatory Compliance

How effectively does the company work with the U.S. Food and Drug Administration (FDA)? Because all drugs sold in the U.S. must first be cleared by this agency, it is critical that a firm is able to work closely with the FDA and satisfy the regulatory authority's drug approval requirements.

Firms with experience navigating the FDA's process and resources to do so are better equipped to obtain regulatory approval. Smaller or newer firms are often less proficient at navigating the process and will often meet major snags in obtaining approval for their products. Managers hired from successful biotech or pharmaceutical firms with proven drug development experience, and/or an alliance with a strong corporate partner, can prove to be invaluable. Increasingly, companies are involving the FDA in trial design and protocol throughout the clinical process to prevent delays and negative surprises in the later stages.

ANALYZING FINANCIAL STATEMENTS

The usefulness of analyzing a biotechnology company's financial statements is often limited, as many biotech companies have little to no earnings history. Because many, if not most, biotech companies are in a developmental stage and have little to no product revenues, traditional financial analysis is of limited value. For these companies, analysts tend to focus on the future earnings potential of products in development and on whether the company has the resources to fully develop those products.

Financial analysis of a large, profitable biotech company tends to be like that of a traditional pharmaceutical firm. Key metrics include revenues, costs and expenses, R&D as a percentage of sales, earnings, margins, growth in earnings per share (EPS), and sales and return on equity (ROE). When possible, individual company statistics should be compared with those of rival companies and the industry average.

Income Statement Analysis

Analysis of the income statement, while still important for biotech firms, provides less insight into future operational trends than for most other industries because biotech firms often have significant investments in products that have yet to be commercialized.

Sales. Sales growth expectations vary among biotech firms depending on what stage their drugs are at. Many biotech companies experience extremely rapid growth following the commercialization of a new drug. On the other hand, firms can also experience rapid declines in sales when they face new competition. Often, this competition can result from the loss of exclusivity for a company's existing product. There are also many publicly traded biotech firms that have little to no sales. Some biotech firms have significant revenue volatility because their revenues are tied to the achievement of certain milestones, *e.g.,* achieving certain results in a phase II trial.

CFRA tries to consider how growth has been achieved, *e.g.,* has growth been generated by unit volume gains, price increases, acquisitions, one-time or non-recurring gains from asset sales, or some combination of these? Is the company gaining market share, or just riding market growth or price hikes?

Watch Out! *When companies accelerate revenue into the current period, the reported revenue growth for that period is likely unsustainable. Management can accelerate revenue by allocating a higher proportion of transaction price to elements delivered upfront in contracts with multiple deliverables or performance obligations, faster recognition of deferred revenue, large shipments at period-end, a change in revenue recognition policy, and a change in the interpretation of the revenue recognition policy.*

Watch Out! *It is common for Biotechnology companies to monetize certain intangible assets by selling the rights to a product to another entity. CFRA views the sale of product rights as the sale of an asset, which should be included in other income, similar to the sale of real property. In instances where these sales are recognized as revenue, gross margins are likely boosted due to the lack of related cost of goods sold.*

Research & development. Significant investment in research & development (R&D) is critical to the success of any biotechnology company. R&D spending is high for the biotechnology industry compared to other industries. For developmental-stage companies that have not yet produced commercial products, R&D typically exceeds any revenues that these companies receive from collaboration agreements. When

comparing companies, most investors look at ratios such as R&D as a percentage of sales, R&D expenditures per employee, or R&D as a percentage of market capitalization.

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 the FDA approves a product. A material increase in capitalized R&D costs not explained by the timing of FDA approval may indicate overcapitalization of R&D, which could pressure future earnings growth.*

SG&A expenses. Royalty costs and costs related to product co-promotion may be included in selling, general, and administrative (SG&A) expenses or another line item. Investors should compare royalty obligations and the financial structure of collaborative arrangements between firms to assess the potential profitability of a drug.

Option expense. Companies are required to expense options in the income statement. Investors should be aware of options grants since an elevated level of outstanding options could dilute EPS if these options are eventually exercised. A considerable number of options outstanding could also divert company cash to repurchasing shares to neutralize the dilutive effect of options. This cash could otherwise be used for product promotion, drug development, or dividends. Many biotechnology companies report earnings excluding stock option expenses, described as “adjusted” or “not in conformity with generally accepted accounting principles” (non-GAAP) earnings.

Profit margins. Margins vary significantly for biotech firms and many companies in the industry are unprofitable. Biotech firms incur substantial costs for extended periods of time while researching and developing drugs, which is why these companies are often able to later sell their products for high prices and achieve high margins once they successfully commercialize their drugs. For most biotech firms, SG&A and R&D expenses tend to be as high as the proportion of revenue when compared to most other companies.

Earnings per share (EPS). Because product pipelines are so critical in the biotech industry, analysts often consider EPS trends that are several years into the future. Changes in the development and commercialization timeline for pipeline products can significantly alter future EPS trends, which is why biotech valuations can change so rapidly. Many young biotech firms often post losses or volatile earnings because they have yet to commercialize any products or are in the initial stages of commercialization, which limits the utility of historical and near-term EPS analysis. Large, well-established biotechnology firms tend to have more stable earnings.

Balance Sheet Analysis

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. For biotechnology companies, most balance sheet analysis focuses on liquidity because biotech firms require liquidity to continue funding their R&D activities. A promising drug candidate is worth near nothing if a company cannot eventually sell it; therefore, it is crucial to assess a company’s ability to fund the development and commercialization of its drugs. Liquidity is especially important in market downturns when funding typically becomes difficult to obtain.

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. For development-stage biotech companies with no earnings, CFRA likes to see at least two years’ worth of cash on hand to fund operations at the current burn rate, i.e., the rate at which cash is being consumed by R&D and other expenditures. Investors should also consider the amount of convertible debt outstanding, if any, since several biotech firms issue convertible notes.

Debt-to-capitalization. This ratio is calculated by dividing debt by total capital (the sum of debt and stockholders’ equity). Companies with lower levels of debt to capital are generally less burdened by interest payments and more capable of raising debt. Biotech firms that are not mature often have little debt

because their typically weak cash flows make it difficult to service interest payments. Investors should investigate sudden changes in a company's attitude toward taking on debt.

Equity Valuation

Biotech companies are notoriously difficult to value because their expected earnings are tied more heavily to future expectations than most other companies. For the few profitable and well-established companies, a price-to-earnings (P/E) ratio can be used to compare a company's valuation versus its peers.

Most publicly traded biotech companies are at the development stage and without near-term commercial prospects. These companies are often valued with some sort of a net present value (NPV) analysis, such as a discounted cash flow (DCF) analysis. An NPV analysis typically gauges the revenue potential for a company's key pipeline candidates, key commercialized products, the costs associated with developing and commercializing those drugs, the probability of successful commercialization, and then discounts the expected profits to the present year.

GLOSSARY

Beta-cetanin—A multifunctional, 90 kD protein that contributes to cell development under normal physiological conditions.

Biologics—Also known as biologic drugs, biologics are medicinal preparations made from living organisms or their byproducts. Vaccines, antigens, serums, and plasmas are examples of biologics.

Biologics license application (BLA)—The formal filing that drug makers submit to the U.S. Food and Drug Administration (FDA) for approval to market new biologics-based drugs. The application must contain clinical evidence of the compound's safety and efficacy.

Biosimilar—A generic copy of a biological molecule, developed using modern biotechnology techniques. A biosimilar has similar activity and is structurally nearly identical to the biologic that it copies. Unlike generic chemical-based drugs, however, a biosimilar is not truly identical and therefore will require a different regulatory process than pharmaceutical generics.

Blockbuster Drugs—An extremely popular drug that generates annual sales of at least $1 billion for the company that sells it.

Breakthrough drug—A compound with a mechanism of action significantly different from that of existing drugs, representing a major therapeutic advance.

CAR T-cell therapy—Chimeric antigen receptor T cells are T cells that have been genetically engineered to produce an artificial T cell receptor for use in immunotherapy.

Cell Therapies—A therapy in which viable cells are injected, grafted, or implanted into a patient in order to effectuate a medicinal effect

Clinical trials—Tests, typically consisting of three stages, in which experimental drugs are administered to humans to determine their safety and efficacy before being submitted for regulatory marketing approval.

Deoxyribonucleic acid (DNA)—The basic molecule that contains genetic information for most living systems. The DNA molecule consists of four nucleotide bases (adenine, cytosine, guanine, and thymine) and a sugar-phosphate frame arranged in two connected strands forming a double helix.

Enzyme—A substance that acts as a catalyst in living organisms, regulating the rate at which chemical reactions proceed without itself being altered in the process.

Gene sequencing—A scientific technique whereby DNA strands are decoded to quantify the exact order of DNA's four nucleotides (A, C, G, and T). This method allows scientists to analyze the sequence of strands and identify specific genes embedded in DNA.

Gene therapy—The introduction of specific genes into a patient's body to replace defective ones or to suppress the action of a harmful one.

Genetic Disorder—A disease caused in whole or in part by a change in the DNA sequence away from the normal sequence.

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

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

Legacy Drugs—Drugs that have been prescribed for at least 25 years and have gained a history for safety and efficacy.

Ligase—An enzyme that brings about ligation of DNA or another substance.

Molecular glue—A small molecule that stabilizes the interaction between two proteins that do not normally interact.

Monoclonal antibodies (mAbs)—Large protein molecules produced by white blood cells, which seek out and destroy harmful foreign substances.

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

New Molecular Entities (NME)—A drug that contains an active moiety that has never been approved by the FDA or marketed in the U.S.

Novel Virus—A virus that has not previously been recorded.

Orphan drug—A drug designed to treat a rare disease afflicting a relatively small patient population (currently fewer than 200,000 cases in the U.S.). The U.S. government provides special incentives to encourage development of such drugs.

Patent thicket—A layer of numerous patents that protect the exclusivity of a drug.

Pharmacy Benefit Managers (PBM)—A third-party administrator of prescription drug programs for commercial health plans, self-insured employer plans, Medicare Part D plans, the Federal Employees Health Benefits Program, and state government employee plans in the U.S.

Phenotypic Plasticity—The ability of an organism to change in response to stimuli or inputs from the environment.

Protein—Any class of nitrogenous organic compounds that have large molecules composed of one or more long chains of amino acids and are an essential part of all living organisms, especially as structural components of body tissues such as muscle, hair, etc., and as enzymes and antibodies.

Recombinant Products—A subset of biologics that are produced by genetic engineering techniques.

Reference Pricing—A system in which an insurer (or other payer such as an employer) selects a price that it is willing to pay for a health care service or procedure.

Specialty Drugs—Often biologics, these drugs are derived from living cells and are used to treat complex or rare chronic conditions such as cancer, rheumatoid arthritis, hemophilia, H.I.V.

Tegavivint—A small molecule inhibitor of the WNT/beta-catenin pathway with potential antineoplastic activity.

Third-Party Payer Reimbursement—A payment for services by an entity other than the patient or the patient's family.

WNT Signaling Pathway—A group of signal transduction pathways that begin with proteins that pass signals into a cell through cell surface receptors.

INDUSTRY REFERENCES

PERIODICALS

Drug Trend Report
https://www.evernorth.com/drug-trend-report
Annual publication with detailed analysis of prescription drug costs and utilization; published by Evernorth, a pharmacy benefit manager.

The Use of Medicines in the U.S. 2022
https://www.iqvia.com/insights/the-iqvia-institute/reports/the-use-of-medicines-in-the-us-2022
Annual trend report from IQVIA covers usage and spending trends of medicines in the U.S.

GOVERNMENT AGENCIES

European Medicines Agency (EMA)
ema.europa.eu/ema
Regulatory body responsible for approvals and oversight of medications in the European Union (EU).

National Human Genome Research Institute (NHGRI)
genome.gov
The NHGRI is an institute under the NIH that carries out the International Human Genome Project (HGP) and to apply genome technologies to the study of specific diseases.

National Institutes of Health (NIH)
nih.gov
Part of U.S. Health & Human Services (HHS), the NIH is the primary federal medical research agency.

U.S. Department of Health and Human Services (HHS)
hhs.gov
Federal agency charged with enhancing and protecting the health and well-being of all Americans.

U.S. Food and Drug Administration (FDA)
fda.gov
Federal agency charged with supervising the U.S. food, pharmaceuticals, and biotechnology industries; part of the U.S. Department of Health and Human Services (HHS).

TRADE ASSOCIATIONS

Biotechnology Innovation Organization (BIO)
bio.org
Represents biotech companies, academic institutions, and state biotech centers in legislative and regulatory affairs; publishes industry statistics and information.

The Henry J. Kaiser Family Foundation (KFF)
kff.org
Nonprofit foundation dedicated to studying and reporting on the U.S. health care system. Publishes reports on government programs, medical spending trends, and various policy initiatives.

Pharmaceutical Research and Manufacturers of America (PhRMA)
phrma.org
Represents prescription drug firms in legislative and regulatory affairs; publishes industry statistics and information.

ONLINE RESOURCES

Amgen
https://www.amgen.com/
An American multinational biopharmaceutical company headquartered in Thousand Oaks, California.

ClinicalTrials.gov
clinicaltrials.gov
A centralized database operated by the NIH, listing information on thousands of public and private clinical drug trials, completed or ongoing, in the U.S.

Financial Times
ft.com
A British daily newspaper printed in broadsheet and published digitally that focuses on business and economic current affairs.

S&P Global Market Intelligence
https://www.spglobal.com/marketintelligence/en/
A division of S&P Global that provides essential intelligence for individuals, companies, and governments to make decisions with confidence.

OTHER SOURCES

Drug Channels Institute
drugchannels.net
Drug Channels Institute analyzes pharmaceutical economics and the drug distribution system in the U.S. and provides insight into the complex U.S. pharmacy distribution and reimbursement system.

Evaluate Ltd.
evaluategroup.com/public/EvaluatePharma-Content.aspx
Provides consensus forecasts and analysis of the pharmaceuticals and biotechnology industries.

Milken Institute
milkeninstitute.org
An independent economic think tank that publishes research and hosts conferences that apply market-based principles and financial innovations.

Tufts Center for the Study of Drug Development (CSDD)
csdd.tufts.edu
A nonprofit academic research group (affiliated with Tufts University) that provides strategic information on the quality and efficiency of pharmaceutical development and utilization.

World Health Organization
who.int
A specialized agency of the United Nations responsible for international public health.

COMPARATIVE COMPANY ANALYSIS

Operating Revenues

Ticker		Company		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
BIOTECHNOLOGY																				
ABBV	[]	ABBVIE INC.		DEC	56,197.0	45,804.0	33,266.0	32,753.0	28,216.0	25,638.0	22,859.0	12.4	17.0	22.7	246	200	146	143	123	112
AMGN	[]	AMGEN INC.		DEC	25,979.0	25,424.0	23,362.0	23,747.0	22,849.0	22,991.0	21,662.0	5.2	2.5	2.2	120	117	108	110	105	106
ANIK	§	ANIKA THERAPEUTICS, INC.		DEC	147.8	130.5	114.6	105.6	113.4	103.4	93.0	8.6	7.4	13.3	159	140	123	114	122	111
ARWR	†	ARROWHEAD PHARMACEUTICALS, INC.		SEP	138.3	88.0	168.8	16.1	31.4	0.2	0.4	84.9	287.5	57.2	36201	23035	44187	4226	8222	41
BIIB	[]	BIOGEN INC.		DEC	10,981.7	13,444.6	14,377.9	13,452.9	12,273.9	11,448.8	10,763.8	8.1	-0.8	-18.3	102	125	134	125	114	106
CHRS	§	COHERUS BIOSCIENCES, INC.		DEC	326.6	475.8	356.1	0.0	1.6	190.1	30.0	NA	11.4	-31.4	1087	1584	1185	0	5	633
CYTK	§	CYTOKINETICS, INCORPORATED		DEC	70.4	55.8	26.9	31.5	13.4	106.4	28.7	33.2	-7.9	26.2	246	195	94	110	47	371
EGRX	§	EAGLE PHARMACEUTICALS, INC.		DEC	171.5	187.8	195.9	213.3	236.7	189.5	66.2	33.5	-2.0	-8.7	259	284	296	322	357	286
EBS	§	EMERGENT BIOSOLUTIONS INC.		DEC	1,792.7	1,555.4	1,106.0	782.4	560.9	488.8	489.3	20.7	29.7	15.3	366	318	226	160	115	100
ENTA	§	ENANTA PHARMACEUTICALS, INC.		SEP	97.1	122.5	205.2	206.6	102.8	88.3	160.9	8.8	1.9	-20.7	60	76	128	128	64	55
EXEL	†	EXELIXIS, INC.		DEC	1,435.0	987.5	967.8	853.8	452.5	191.5	37.2	17.4	49.6	45.3	3860	2657	2604	2297	1217	515
GILD	[]	GILEAD SCIENCES, INC.		DEC	27,305.0	24,689.0	22,449.0	22,127.0	26,107.0	30,390.0	32,639.0	12.5	-2.1	10.6	84	76	69	68	80	93
HALO	†	HALOZYME THERAPEUTICS, INC.		DEC	443.3	267.6	196.0	151.9	316.6	146.7	135.1	23.0	24.8	65.7	328	198	145	112	234	109
INCY	[]	INCYTE CORPORATION		DEC	2,986.3	2,666.7	2,158.8	1,881.9	1,536.2	1,105.7	753.8	41.3	22.0	12.0	396	354	286	250	204	147
LGND	§	LIGAND PHARMACEUTICALS INCORPORATED		DEC	277.1	186.4	120.3	251.5	141.1	109.0	71.9	24.9	20.5	48.7	385	259	167	350	196	152
MYGN	§	MYRIAD GENETICS, INC.		DEC	690.6	557.0	851.1	743.7	728.7	740.5	723.1	5.6	-1.4	24.0	96	77	118	103	101	102
REGN	[]	REGENERON PHARMACEUTICALS, INC.		DEC	16,071.7	8,497.1	6,557.6	5,145.6	5,872.2	4,860.4	4,103.7	43.1	27.0	89.1	392	207	160	125	143	118
RGNX	§	REGENXBIO INC.		DEC	470.3	154.6	35.2	218.5	10.4	4.6	7.6	NA	152.4	204.3	6199	2037	464	2880	137	60
SPPI		SPECTRUM PHARMACEUTICALS, INC.	#	JAN	0.0	0.0	0.0	0.0	0.0	146.4	162.6	NA	NA	NA	0	0	0	0	0	90
UTHR	†	UNITED THERAPEUTICS CORPORATION		DEC	1,685.5	1,483.3	1,448.8	1,627.8	1,725.3	1,598.8	1,465.8	8.5	1.1	13.6	115	101	99	111	118	109
VNDA	§	VANDA PHARMACEUTICALS INC.		DEC	268.7	248.2	227.2	193.1	165.1	146.0	109.9	24.0	13.0	8.3	244	226	207	176	150	133
VRTX	[]	VERTEX PHARMACEUTICALS INCORPORATEI		DEC	7,574.4	6,205.7	4,162.8	3,047.6	2,488.7	1,702.2	1,032.3	18.3	34.8	22.1	734	601	403	295	241	165
XNCR	§	XENCOR, INC.		DEC	275.1	122.7	156.7	40.6	46.2	109.0	27.8	44.7	20.3	124.2	991	442	564	146	166	393

Note: Data as originally reported. CAGR-Compound annual growth rate.
[]Company included in the S&P 500. †Company included in the S&P MidCap 400. §Company included in the S&P SmallCap 600. #Of the following calendar year.
Souce: S&P Capital IQ.

Net Income

Ticker		Company	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
BIOTECHNOLOGY																			
ABBV	[]	ABBVIE INC.	DEC	11,542.0	4,616.0	7,882.0	5,687.0	5,309.0	5,953.0	5,144.0	12.9	14.2	150.0	224	90	153	111	103	116
AMGN	[]	AMGEN INC.	DEC	5,893.0	7,264.0	7,842.0	8,394.0	1,979.0	7,722.0	6,939.0	4.8	-5.3	-18.9	85	105	113	121	29	111
ANIK	§	ANIKA THERAPEUTICS, INC.	DEC	4.1	-24.0	27.2	18.7	31.8	32.5	30.8	-6.9	-33.8	NM	13	-78	88	61	103	106
ARWR	†	ARROWHEAD PHARMACEUTICALS, INC.	SEP	-140.8	-84.6	68.0	-54.5	-34.4	-81.7	-91.9	46.3	11.5	66.6	153	92	-74	59	37	89
BIIB	[]	BIOGEN INC.	DEC	1,556.1	4,000.6	5,888.5	4,430.7	2,539.1	3,702.8	3,547.0	2.3	-15.9	-61.1	44	113	166	125	72	104
CHRS	§	COHERUS BIOSCIENCES, INC.	DEC	-287.1	132.2	89.8	-209.3	-238.2	-127.3	-223.3	NA	17.7	NM	129	-59	-40	94	107	57
CYTK	§	CYTOKINETICS, INCORPORATED	DEC	-215.3	-127.3	-121.7	-106.3	-127.8	16.5	-37.5	16.2	NM	69.2	574	339	325	283	341	-44
EGRX	§	EAGLE PHARMACEUTICALS, INC.	DEC	-8.6	12.0	14.3	31.9	51.9	81.5	2.6	5.3	NM	NM	-336	466	557	1241	2020	3168
EBS	§	EMERGENT BIOSOLUTIONS INC.	DEC	230.9	305.1	54.5	62.7	82.6	51.8	62.9	25.9	34.8	-24.3	367	485	87	100	131	82
ENTA	§	ENANTA PHARMACEUTICALS, INC.	SEP	-79.0	-36.2	46.4	72.0	17.7	21.7	79.0	NA	NM	118.4	-100	-46	59	91	22	27
EXEL	†	EXELIXIS, INC.	DEC	231.1	111.8	321.0	690.1	154.2	-70.2	-161.7	11.8	NM	106.7	-143	-69	-198	-427	-95	43
GILD	[]	GILEAD SCIENCES, INC.	DEC	6,225.0	123.0	5,386.0	5,455.0	4,628.0	13,501.0	18,108.0	8.3	-14.3	4,961.0	34	1	30	30	26	75
HALO	†	HALOZYME THERAPEUTICS, INC.	DEC	402.7	129.1	-72.2	-80.3	63.0	-103.0	-32.2	NA	NM	212.0	NM	-400	224	249	-195	320
INCY	[]	INCYTE CORPORATION	DEC	948.6	-295.7	446.9	109.5	-313.1	104.2	6.5	NA	55.5	NM	14524	NM	6843	1677	NM	1596
LGND	§	LIGAND PHARMACEUTICALS INCORPORATED	DEC	57.1	-3.0	629.3	143.3	12.6	-1.6	229.8	19.4	NM	NM	25	-1	274	62	5	-1
MYGN	§	MYRIAD GENETICS, INC.	DEC	-27.2	-223.7	4.6	133.3	17.4	117.2	80.2	NA	NM	-87.8	-34	-279	6	166	22	146
REGN	[]	REGENERON PHARMACEUTICALS, INC.	DEC	8,075.3	3,513.2	2,115.8	2,444.4	1,198.5	895.5	636.1	NA	55.2	129.9	1270	552	333	384	188	141
RGNX	§	REGENXBIO INC.	DEC	127.8	-111.3	-94.7	99.9	-73.2	-63.0	-22.8	NA	NM	NM	-560	488	415	-438	321	276
SPPI		SPECTRUM PHARMACEUTICALS, INC.	# JAN	0.0	-160.9	-112.7	-120.7	-92.2	-69.8	-52.6	NA	NA	NA	0	306	214	229	175	133
UTHR	†	UNITED THERAPEUTICS CORPORATION	DEC	475.8	514.8	-104.5	589.2	417.9	713.7	651.6	8.1	-7.8	-7.6	73	79	-16	90	64	110
VNDA	§	VANDA PHARMACEUTICALS INC.	DEC	33.2	23.3	115.6	25.2	-15.6	-18.0	-39.9	NA	NM	42.1	-83	-59	-290	-63	39	45
VRTX	[]	VERTEX PHARMACEUTICALS INCORPORATED	DEC	2,342.1	2,711.7	1,176.8	2,096.9	263.5	-112.1	-556.3	54.8	NM	-13.6	-421	-487	-212	-377	-47	20
XNCR	§	XENCOR, INC.	DEC	82.6	-69.3	26.9	-70.4	-38.5	45.1	-17.6	NA	12.9	NM	-470	394	-153	400	219	-257

Note: Data as originally reported. CAGR-Compound annual growth rate.
[]Company included in the S&P 500. †Company included in the S&P MidCap 400. §Company included in the S&P SmallCap 600. #Of the following calendar year.
Souce: S&P Capital IQ.

				Return on Revenues (%)						Return on Assets (%)						Return on Equity (%)					
Ticker		**Company**	**Yr. End**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**
BIOTECHNOLOGY																					
ABBV	[]	ABBVIE INC.	DEC	20.5	10.1	23.7	17.4	18.8	23.2	7.9	3.1	8.8	9.6	7.5	9.0	81.0	187.7	NM	NM	109.1	138.7
AMGN	[]	AMGEN INC.	DEC	22.7	28.6	33.6	35.3	8.7	33.6	9.6	11.5	13.1	12.6	2.5	9.9	73.2	76.1	70.7	44.5	7.2	26.6
ANIK	§	ANIKA THERAPEUTICS, INC.	DEC	2.8	NM	23.7	17.7	28.1	31.5	1.2	NM	8.2	6.7	11.3	13.5	1.5	NM	9.9	7.1	13.1	15.0
ARWR	†	ARROWHEAD PHARMACEUTICALS, INC.	SEP	NM	NM	40.3	NM	NM	NM	NM	NM	19.4	NM	NM	NM	NM	NM	40.1	NM	NM	NM
BIIB	[]	BIOGEN INC.	DEC	14.2	29.8	41.0	32.9	20.7	32.3	6.5	16.3	21.6	17.5	10.7	16.2	16.0	33.8	44.7	34.9	21.6	34.4
CHRS	§	COHERUS BIOSCIENCES, INC.	DEC	NM	27.8	25.2	0.0	NM	NM	NM	15.7	22.0	NM	NM	NM	NM	68.5	269.7	NM	NM	NM
CYTK	§	CYTOKINETICS, INCORPORATED	DEC	NM	NM	NM	NM	NM	15.5	NM	NM	NM	NM	NM	9.7	NM	NM	NM	NM	NM	20.2
EGRX	§	EAGLE PHARMACEUTICALS, INC.	DEC	NM	6.4	7.3	15.0	21.9	43.0	NM	4.7	5.6	13.4	19.2	38.0	NM	6.6	8.4	18.8	31.4	67.4
EBS	§	EMERGENT BIOSOLUTIONS INC.	DEC	12.9	19.6	4.9	8.0	14.7	10.6	7.8	10.6	2.3	2.8	7.7	5.3	15.1	24.1	5.2	6.5	11.0	10.0
ENTA	§	ENANTA PHARMACEUTICALS, INC.	SEP	NM	NM	22.6	34.8	17.2	24.5	NM	NM	9.5	17.4	5.4	7.7	NM	NM	10.8	20.7	6.2	8.5
EXEL	†	EXELIXIS, INC.	DEC	16.1	11.3	33.2	80.8	34.1	NM	8.8	5.2	17.0	48.5	23.5	NM	11.3	6.3	21.6	87.8	82.4	NM
GILD	[]	GILEAD SCIENCES, INC.	DEC	22.8	0.5	24.0	24.7	17.7	44.4	9.2	0.2	8.7	8.6	6.6	23.7	31.6	0.4	24.3	26.0	23.3	70.1
HALO	†	HALOZYME THERAPEUTICS, INC.	DEC	90.8	48.2	NM	NM	19.9	NM	36.5	22.3	NM	NM	12.1	NM	231.4	106.3	NM	NM	71.6	NM
INCY	[]	INCYTE CORPORATION	DEC	31.8	NM	20.7	5.8	NM	9.4	19.2	NM	13.0	4.1	NM	6.4	29.7	NM	19.8	6.2	NM	35.3
LGND	§	LIGAND PHARMACEUTICALS INCORPORATED	DEC	20.6	NM	523.2	57.0	8.9	NM	4.4	NM	42.1	11.4	1.9	NM	7.5	NM	94.8	29.3	3.2	NM
MYGN	§	MYRIAD GENETICS, INC.	DEC	NM	NM	0.5	17.9	2.4	15.8	NM	NM	0.3	11.3	1.4	13.3	NM	0.0	0.4	15.4	2.3	16.6
REGN	[]	REGENERON PHARMACEUTICALS, INC.	DEC	50.2	41.3	32.3	47.5	20.4	18.4	31.7	20.5	14.3	20.8	13.7	12.8	54.2	31.8	21.3	32.8	22.6	22.1
RGNX	§	REGENXBIO INC.	DEC	27.2	NM	NM	45.7	NM	NM	11.5	NM	NM	18.4	NM	NM	22.4	NM	NM	28.9	NM	NM
SPPI		SPECTRUM PHARMACEUTICALS, INC.	# JAN	0.0	0.0	0.0	0.0	0.0	0.0	NA	NA	NM	NM	NM	NM	0.0	0.0	NM	NM	NM	NM
UTHR	†	UNITED THERAPEUTICS CORPORATION	DEC	28.2	34.7	NM	36.2	24.2	44.6	9.2	11.2	NM	17.3	14.5	30.7	12.9	16.7	NM	24.1	21.1	41.5
VNDA	§	VANDA PHARMACEUTICALS INC.	DEC	12.3	9.4	50.9	13.1	NM	NM	5.6	4.4	23.9	7.6	NM	NM	6.9	5.4	33.7	12.4	NM	NM
VRTX	[]	VERTEX PHARMACEUTICALS INCORPORATED	DEC	30.9	43.7	28.3	68.8	10.6	NM	17.4	23.1	14.1	33.6	7.4	NM	24.9	36.7	22.4	64.4	5.4	NM
XNCR	§	XENCOR, INC.	DEC	30.0	NM	17.2	NM	NM	41.4	9.9	NM	4.0	NM	NM	10.5	12.7	NM	4.8	NM	NM	18.9

Note: Data as originally reported. CAGR-Compound annual growth rate.
[]Company included in the S&P 500. †Company included in the S&P MidCap 400. §Company included in the S&P SmallCap 600. #Of the following calendar year.
Souce: S&P Capital IQ.

				Current Ratio						Debt/Capital Ratio (%)						Debt as a % of Net Working Capital					
Ticker		**Company**	**Yr. End**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**
BIOTECHNOLOGY																					
ABBV	[]	ABBVIE INC.	DEC	0.8	0.8	3.2	1.0	1.3	1.7	80.6	85.6	114.9	145.7	87.0	89.6	NM	NM	185.7	NM	684.3	574.7
AMGN	[]	AMGEN INC.	DEC	1.6	1.8	1.4	2.8	5.5	4.1	83.2	77.8	73.6	70.2	57.5	57.6	461.4	346.6	480.8	122.3	84.5	99.4
ANIK	§	ANIKA THERAPEUTICS, INC.	DEC	5.7	4.8	14.4	18.0	15.8	19.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ARWR	†	ARROWHEAD PHARMACEUTICALS, INC.	SEP	2.6	7.9	2.7	6.4	3.6	3.5	0.0	0.0	0.0	2.2	2.8	2.6	0.0	0.0	0.0	3.2	4.7	3.9
BIIB	[]	BIOGEN INC.	DEC	1.8	1.8	1.7	2.3	2.3	2.6	36.4	41.0	25.1	31.3	32.0	34.9	176.3	236.1	126.7	136.6	131.7	122.6
CHRS	§	COHERUS BIOSCIENCES, INC.	DEC	3.6	5.3	3.0	2.5	5.1	2.9	80.7	59.0	62.9	159.8	76.9	83.8	93.4	65.0	78.2	201.5	86.8	95.4
CYTK	§	CYTOKINETICS, INCORPORATED	DEC	7.5	15.2	9.0	9.4	8.5	4.8	36.9	54.5	109.2	60.6	22.4	22.5	30.8	30.6	62.2	21.5	13.1	21.8
EGRX	§	EAGLE PHARMACEUTICALS, INC.	DEC	2.3	4.4	4.6	4.1	4.0	2.7	0.0	11.9	15.8	19.2	19.3	0.0	0.0	19.6	23.9	30.7	30.3	0.0
EBS	§	EMERGENT BIOSOLUTIONS INC.	DEC	3.4	3.1	3.2	3.1	4.8	4.8	33.4	37.0	42.4	43.7	1.5	31.8	90.3	104.8	170.3	186.6	3.5	66.3
ENTA	§	ENANTA PHARMACEUTICALS, INC.	SEP	8.8	18.1	17.8	23.7	11.3	29.4	0.4	0.3	0.4	0.4	0.3	0.1	0.5	0.4	0.4	0.4	0.4	0.1
EXEL	†	EXELIXIS, INC.	DEC	5.4	7.1	7.1	8.5	4.2	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
GILD	[]	GILEAD SCIENCES, INC.	DEC	1.3	1.4	3.1	3.4	2.7	2.1	54.4	61.1	49.4	53.3	63.4	57.6	796.3	622.9	107.6	97.4	161.2	254.1
HALO	†	HALOZYME THERAPEUTICS, INC.	DEC	7.9	1.3	6.3	2.9	3.9	4.7	80.0	0.0	80.7	12.3	37.5	119.5	97.3	0.0	83.7	12.5	33.0	98.7
INCY	[]	INCYTE CORPORATION	DEC	3.7	3.7	4.8	4.3	4.0	3.6	0.0	0.0	0.0	0.9	1.0	60.8	0.0	0.0	0.0	1.2	1.5	90.4
LGND	§	LIGAND PHARMACEUTICALS INCORPORATED	DEC	11.2	5.0	66.1	10.6	1.0	0.7	28.1	38.4	45.4	52.1	0.0	0.0	75.8	110.4	57.7	77.4	0.0	0.0
MYGN	§	MYRIAD GENETICS, INC.	DEC	2.4	2.7	3.0	3.2	1.4	4.3	0.0	20.3	17.7	1.0	11.4	0.0	0.0	92.3	101.2	4.1	117.7	0.0
REGN	[]	REGENERON PHARMACEUTICALS, INC.	DEC	3.6	3.6	3.7	4.5	3.8	2.6	9.5	15.2	0.0	0.0	0.0	0.0	19.6	27.9	0.0	0.0	0.0	0.0
RGNX	§	REGENXBIO INC.	DEC	4.0	6.5	10.2	15.2	11.6	9.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SPPI		SPECTRUM PHARMACEUTICALS, INC.	# JAN	0.0	0.0	3.5	3.9	2.5	2.5	NA	NA	0.0	0.0	0.0	0.0	NA	NA	0.0	0.0	0.0	0.0
UTHR	†	UNITED THERAPEUTICS CORPORATION	DEC	7.6	6.7	4.0	6.4	3.3	4.3	16.8	19.1	17.7	8.2	10.6	0.0	39.6	43.4	42.8	16.8	24.9	0.0
VNDA	§	VANDA PHARMACEUTICALS INC.	DEC	6.4	6.2	6.0	5.6	2.4	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
VRTX	[]	VERTEX PHARMACEUTICALS INCORPORATED	DEC	4.5	4.3	3.6	3.4	3.3	2.3	0.0	0.0	0.0	0.0	0.0	22.4	0.0	0.0	0.0	0.0	0.0	28.9
XNCR	§	XENCOR, INC.	DEC	6.0	5.3	8.4	5.9	3.2	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Note: Data as originally reported. CAGR-Compound annual growth rate.
[]Company included in the S&P 500. †Company included in the S&P MidCap 400. §Company included in the S&P SmallCap 600. #Of the following calendar year.
Souce: S&P Capital IQ.

Ticker		Company	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
BIOTECHNOLOGY																					
ABBV	[]	ABBVIE INC.	DEC	21 - 16	40 - 24	17 - 12	34 - 21	30 - 18	18 - 14	80.2	167.2	80.8	98.1	77.4	62.4	4.9 - 3.7	5.1 - 4.3	7.3 - 4.7	6.8 - 4.6	5.4 - 2.3	4.3 - 2.7
AMGN	[]	AMGEN INC.	DEC	25 - 19	21 - 15	19 - 13	16 - 13	71 - 54	17 - 13	68.1	51.7	44.7	41.8	170.0	38.8	3.5 - 2.9	3.5 - 2.5	3.5 - 2.5	3.5 - 2.5	3.2 - 2.5	3.1 - 2.4
ANIK	§	ANIKA THERAPEUTICS, INC.	DEC	167 - 113	NM - NM	38 - 15	53 - 22	27 - 19	24 - 16	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
ARWR	†	ARROWHEAD PHARMACEUTICALS, INC.	SEP	NM - NM	NM - NM	48 - 15	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
BIIB	[]	BIOGEN INC.	DEC	40 - 21	14 - 10	11 - 7	18 - 12	29 - 21	19 - 13	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
CHRS	§	COHERUS BIOSCIENCES, INC.	DEC	NM - NM	12 - 6	18 - 7	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
CYTK	§	CYTOKINETICS, INCORPORATED	DEC	NM - NM	NM - NM	NM - NM	NM - NM	NM - NM	30 - 15	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
EGRX	§	EAGLE PHARMACEUTICALS, INC.	DEC	NM - NM	68 - 39	62 - 37	39 - 17	28 - 14	17 - 6	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
EBS	§	EMERGENT BIOSOLUTIONS INC.	DEC	29 - 8	23 - 9	63 - 38	59 - 36	24 - 14	34 - 19	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
ENTA	§	ENANTA PHARMACEUTICALS, INC.	SEP	NM - NM	NM - NM	45 - 25	34 - 12	49 - 24	36 - 18	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
EXEL	†	EXELIXIS, INC.	DEC	35 - 22	76 - 40	23 - 14	14 - 6	59 - 28	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
GILD	[]	GILEAD SCIENCES, INC.	DEC	15 - 11	858 - 583	17 - 15	21 - 14	24 - 18	10 - 7	57.9	2804.1	59.8	54.5	59.0	18.2	5.0 - 3.9	4.8 - 3.9	4.7 - 3.2	4.1 - 3.2	3.5 - 2.3	3.2 - 2.4
HALO	†	HALOZYME THERAPEUTICS, INC.	DEC	18 - 11	46 - 15	NM - NM	NM - NM	45 - 21	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
INCY	[]	INCYTE CORPORATION	DEC	23 - 15	NM - NM	46 - 30	196 - 113	NM - NM	200 - 114	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
LGND	§	LIGAND PHARMACEUTICALS INCORPORATEI	DEC	63 - 29	NM - NM	4 - 3	41 - 19	246 - 168	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
MYGN	§	MYRIAD GENETICS, INC.	DEC	NM - NM	NM - NM	752 - 334	26 - 14	146 - 60	26 - 10	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
REGN	[]	REGENERON PHARMACEUTICALS, INC.	DEC	9 - 6	20 - 10	23 - 14	18 - 13	47 - 30	64 - 39	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
RGNX	§	REGENXBIO INC.	DEC	17 - 10	NM - NM	NM - NM	27 - 8	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
SPPI		SPECTRUM PHARMACEUTICALS, INC.	# JAN	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
UTHR	†	UNITED THERAPEUTICS CORPORATION	DEC	20 - 14	13 - 7	NM - NM	11 - 7	18 - 12	10 - 6	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
VNDA	§	VANDA PHARMACEUTICALS INC.	DEC	36 - 22	39 - 17	14 - 6	63 - 28	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
VRTX	[]	VERTEX PHARMACEUTICALS INCORPORATE	DEC	27 - 19	29 - 19	49 - 35	23 - 18	157 - 70	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
XNCR	§	XENCOR, INC.	DEC	38 - 22	NM - NM	97 - 59	NM - NM	NM - NM	26 - 9	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

Note: Data as originally reported. CAGR-Compound annual growth rate.
[]Company included in the S&P 500. †Company included in the S&P MidCap 400. §Company included in the S&P SmallCap 600. #Of the following calendar year.
Souce: S&P Capital IQ.

				Earnings per Share ($)						ngible Book Value per Share (						Share Price (High-Low, $)					
Ticker		Company	Yr. End	2021	2020	2019	2018	2017	2016	2021	2020	2019	2018	2017	2016	2021	2020	2019	2018	2017	2016
BIOTECHNOLOGY																					
ABBV	[]	ABBVIE INC.	DEC	6.5	2.7	5.3	3.7	3.3	3.6	-52.5	-58.3	-28.7	-30.7	-24.0	-24.9	136.8 - 101.8	109.2 - 62.6	92.3 - 62.7	125.9 - 77.5	99.1 - 59.3	68.1 - 50.7
AMGN	[]	AMGEN INC.	DEC	10.3	12.3	12.9	12.6	2.7	10.2	-41.9	-37.8	-41.3	-15.3	2.6	6.6	276.7 - 198.6	265.0 - 177.1	245.0 - 166.3	210.2 - 163.3	191.1 - 147.1	176.9 - 133.6
ANIK	§	ANIKA THERAPEUTICS, INC.	DEC	0.3	-1.7	1.9	1.3	2.1	2.2	13.6	12.1	19.1	17.4	16.7	14.0	48.4 - 32.3	55.1 - 22.0	75.7 - 29.0	69.8 - 28.5	60.3 - 41.6	55.0 - 35.1
ARWR	†	ARROWHEAD PHARMACEUTICALS, INC.	SEP	-1.4	-0.8	0.7	-0.7	-0.5	-1.3	3.8	4.4	2.4	0.9	0.8	1.1	93.7 - 57.9	86.8 - 19.5	73.7 - 11.7	22.4 - 3.6	4.5 - 1.4	8.2 - 1.2
BIIB	[]	BIOGEN INC.	DEC	10.4	24.8	31.4	21.6	11.9	16.9	19.8	12.2	23.3	21.4	19.4	21.6	468.6 - 221.7	375.0 - 223.3	344.0 - 215.8	388.7 - 249.2	348.8 - 244.3	333.7 - 223.0
CHRS	§	COHERUS BIOSCIENCES, INC.	DEC	-3.8	1.6	1.2	-3.2	-4.5	-3.0	1.2	3.8	1.4	-0.6	0.5	0.4	22.2 - 12.2	23.0 - 10.9	23.9 - 8.3	20.7 - 8.4	29.6 - 8.1	32.0 - 12.0
CYTK	§	CYTOKINETICS, INCORPORATED	DEC	-2.8	-2.0	-2.1	-2.0	-2.6	0.4	2.9	1.6	-0.2	0.5	2.0	2.3	47.9 - 17.7	30.1 - 8.0	14.9 - 5.8	10.3 - 5.9	17.2 - 7.0	13.0 - 6.0
EGRX	§	EAGLE PHARMACEUTICALS, INC.	DEC	-0.7	0.9	1.0	2.1	3.3	5.0	9.9	10.2	9.1	7.4	7.8	5.1	58.3 - 36.5	60.7 - 33.8	64.9 - 38.4	85.7 - 36.0	97.2 - 45.1	88.5 - 33.0
EBS	§	EMERGENT BIOSOLUTIONS INC.	DEC	4.3	5.7	1.0	1.2	1.7	1.1	15.4	9.7	1.5	-1.2	15.1	12.8	127.2 - 29.9	137.6 - 46.4	67.5 - 39.1	73.9 - 42.7	47.9 - 27.9	44.4 - 24.5
ENTA	§	ENANTA PHARMACEUTICALS, INC.	SEP	-3.9	-1.8	2.2	3.5	0.9	1.1	19.7	22.7	23.5	20.3	15.8	14.2	102.0 - 40.4	62.1 - 38.4	106.8 - 57.2	127.8 - 52.4	59.9 - 25.9	35.1 - 20.4
EXEL	†	EXELIXIS, INC.	DEC	0.7	0.4	1.0	2.2	0.5	-0.3	6.7	5.8	5.3	4.1	0.7	0.1	25.8 - 15.5	27.8 - 13.7	25.3 - 15.0	32.2 - 13.4	32.5 - 14.2	18.3 - 3.6
GILD	[]	GILEAD SCIENCES, INC.	DEC	4.9	0.1	4.2	4.2	3.5	9.9	-16.5	-18.4	3.7	1.2	-0.6	6.7	74.1 - 57.9	86.0 - 56.6	70.5 - 60.9	89.5 - 60.3	86.3 - 63.8	103.1 - 70.8
HALO	†	HALOZYME THERAPEUTICS, INC.	DEC	2.7	0.9	-0.5	-0.6	0.5	-0.8	1.4	1.1	0.7	1.7	1.5	-0.3	56.4 - 31.8	44.5 - 12.7	19.7 - 13.8	21.5 - 13.2	21.1 - 9.7	17.5 - 7.0
INCY	[]	INCYTE CORPORATION	DEC	4.3	-1.4	2.1	0.5	-1.5	0.5	15.7	10.4	10.4	7.3	5.9	0.0	101.5 - 61.9	110.4 - 62.5	96.8 - 62.0	102.6 - 57.0	153.2 - 92.9	110.0 - 55.0
LGND	§	LIGAND PHARMACEUTICALS INCORPORATED	DEC	3.3	-0.2	31.9	6.0	0.5	-0.1	4.7	-5.4	26.2	10.7	4.0	3.3	219.8 - 98.6	127.8 - 57.2	145.0 - 84.5	278.6 - 128.2	149.3 - 95.1	139.8 - 82.1
MYGN	§	MYRIAD GENETICS, INC.	DEC	-0.4	-3.0	0.1	1.9	0.3	1.6	4.0	-0.4	-0.2	2.7	-0.6	4.7	37.0 - 19.5	30.1 - 9.2	48.4 - 20.1	50.4 - 26.8	37.3 - 15.2	43.7 - 15.9
REGN	[]	REGENERON PHARMACEUTICALS, INC.	DEC	72.0	30.5	18.5	21.3	10.3	7.7	176.1	106.0	101.6	80.7	57.1	42.2	686.6 - 441.0	664.6 - 328.1	442.0 - 271.4	416.5 - 281.9	543.6 - 340.1	532.9 - 325.4
RGNX	§	REGENXBIO INC.	DEC	2.9	-3.0	-2.6	2.7	-2.5	-2.4	17.8	10.1	12.2	14.1	5.8	6.1	50.3 - 27.0	55.0 - 20.0	63.2 - 30.4	85.1 - 23.3	36.1 - 16.3	24.6 - 7.1
SPPI		SPECTRUM PHARMACEUTICALS, INC.	# JAN	0.0	0.0	-1.3	-1.0	-1.2	-1.1	0.0	0.0	0.9	1.7	2.5	2.0	4.5 - 1.2	5.2 - 1.7	12.2 - 3.5	25.3 - 6.2	22.0 - 4.3	7.7 - 3.2
UTHR	†	UNITED THERAPEUTICS CORPORATION	DEC	10.1	11.5	-2.4	13.4	9.3	15.3	86.8	72.7	59.7	60.1	47.6	42.3	218.4 - 150.7	152.8 - 75.6	128.9 - 74.3	152.6 - 100.1	169.9 - 112.0	160.0 - 97.5
VNDA	§	VANDA PHARMACEUTICALS INC.	DEC	0.6	0.4	2.1	0.5	-0.4	-0.4	8.7	7.9	7.2	4.8	2.3	2.4	21.9 - 13.1	17.0 - 7.1	31.3 - 11.8	33.4 - 13.8	19.0 - 11.9	18.0 - 6.9
VRTX	[]	VERTEX PHARMACEUTICALS INCORPORATED	DEC	9.0	10.3	4.5	8.1	1.0	-0.5	34.2	28.0	18.1	17.2	7.7	3.3	243.0 - 176.4	306.1 - 197.5	225.7 - 161.0	194.9 - 144.1	167.9 - 73.3	125.0 - 71.5
XNCR	§	XENCOR, INC.	DEC	1.4	-1.2	0.5	-1.3	-0.8	1.1	12.1	9.6	10.2	9.1	6.5	6.5	58.3 - 30.1	47.9 - 19.4	46.3 - 27.8	48.4 - 20.2	28.6 - 18.6	29.4 - 9.9

Note: Data as originally reported. CAGR-Compound annual growth rate.
[]Company included in the S&P 500. †Company included in the S&P MidCap 400. §Company included in the S&P SmallCap 600. #Of the following calendar year.
Souce: S&P Capital IQ.

Disclosures

CFRA's Industry Surveys Reports (the "Industry Surveys") have been prepared by Accounting Research & Analytics, LLC and/or one of its affiliates. The Industry Surveys are published and originally distributed by Accounting Research & Analytics, LLC d/b/a CFRA ("CFRA US"), with the following exceptions: In the United Kingdom/European Union/European Economic Area, the Industry Surveys are published and originally distributed by CFRA U.K. Limited (company number 08456139 registered in England & Wales with its registered office address at New Derwent House, 69-73 Theobalds Road, London, WC1X 8TA, United Kingdom), which is regulated by the U.K. Financial Conduct Authority (No. 775151); in Malaysia, the Industry Surveys are published and originally distributed by CFRA MY Sdn Bhd (Company No. 683377-A) and regulated by Securities Commission Malaysia, No. CMSL/A0181/2007 ("CFRA Malaysia"). CFRA Malaysia is a wholly-owned subsidiary of CFRA US. For Recipients in Canada: This report is not prepared subject to Canadian disclosure requirements and may not be suitable for Canadian investors.

The content of this report and the opinions expressed herein are those of CFRA based upon publicly-available information that CFRA believes to be reliable and the opinions are subject to change without notice. This analysis has not been submitted to, nor received approval from, the United States Securities and Exchange Commission or any other regulatory body. While CFRA exercised due care in compiling this analysis, CFRA AND ALL RELATED ENTITIES SPECIFICALLY DISCLAIM ALL WARRANTIES, EXPRESS OR IMPLIED, to the full extent permitted by law, regarding the accuracy, completeness, or usefulness of this information and assumes no liability with respect to the consequences of relying on this information for investment or other purposes.

No content (including ratings, credit-related analyses and data, valuations, model, software or other application or output therefrom) or any part thereof (Content) may be modified, reverse engineered, reproduced or distributed in any form by any means, or stored in a database or retrieval system, without the prior written permission of CFRA. The Content shall not be used for any unlawful or unauthorized purposes. CFRA and any third-party providers, as well as their directors, officers, shareholders, employees or agents do not guarantee the accuracy, completeness, timeliness or availability of the Content.

Past performance is not necessarily indicative of future results. This document may contain forward-looking statements or forecasts; such forecasts are not a reliable indicator of future performance.

This report is not intended to, and does not, constitute an offer or solicitation to buy and sell securities or engage in any investment activity. This report is for informational purposes only. Recommendations in this report are not made with respect to any particular investor or type of investor. Securities, financial instruments or strategies mentioned herein may not be suitable for all investors and this material is not intended for any specific investor and does not take into account an investor's particular investment objectives, financial situations or needs. Before acting on any recommendation in this material, you should consider whether it is suitable for your particular circumstances and, if necessary, seek professional advice.

CFRA may license certain intellectual property or provide services to, or otherwise have a business relationship with, certain issuers of securities that are the subject of CFRA research reports, including exchange-traded investments whose investment objective is to substantially replicate the returns of a proprietary index of CFRA. In cases where CFRA is paid fees that are tied to the amount of assets invested in a fund or the volume of trading activity in a fund, investment in the fund may result in CFRA receiving compensation in addition to the subscription fees or other compensation for services rendered by CFRA, however, no part of CFRA's compensation for services is tied to any recommendation or rating. Additional information on a subject company may be available upon request.

CFRA's financial data provider is S&P Global Market Intelligence. THIS DOCUMENT CONTAINS COPYRIGHTED AND TRADE SECRET MATERIAL DISTRIBUTED UNDER LICENSE FROM S&P GLOBAL MARKET INTELLIGENCE. FOR RECIPIENT'S INTERNAL USE ONLY.

The Global Industry Classification Standard (GICS®) was developed by and/or is the exclusive property of MSCI, Inc. and S&P Global Market Intelligence. GICS is a service mark of MSCI and S&P Global Market Intelligence and has been licensed for use by CFRA.

Certain information in this report is provided by S&P Global, Inc. and/or its affiliates and subsidiaries (collectively "S&P Global"). Such information is subject to the following disclaimers and notices: "Copyright © 2022, S&P Global Market Intelligence (and its affiliates as applicable). All rights reserved. Nothing contained herein is investment advice and a reference to a particular investment or security, a credit rating or any observation concerning a security or investment provided by S&P Global is not a recommendation to buy, sell or hold such investment or security or make any other investment decisions. This may contain information obtained from third parties, including ratings from credit ratings agencies. Reproduction and distribution of S&P Global's information and third-party content in any form is prohibited except with the prior written permission of S&P Global or the related third party, as applicable. Neither S&P Global nor its third-party providers guarantee the accuracy, completeness, timeliness or availability of any information, including ratings, and are not responsible for any errors or omissions (negligent or otherwise), regardless of the cause, or for the results obtained from the use of such information or content. S&P GLOBAL AND ITS THIRD-PARTY CONTENT PROVIDERS GIVE NO EXPRESS OR IMPLIED WARRANTIES, INCLUDING, BUT NOT LIMITED TO, ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR

PURPOSE OR USE AND ALL S&P INFORMATION IS PROVIDED ON AN AS-IS BASIS. S&P GLOBAL AND ITS THIRD-PARTY CONTENT PROVIDERS SHALL NOT BE LIABLE FOR ANY DIRECT, INDIRECT, INCIDENTAL, EXEMPLARY, COMPENSATORY, PUNITIVE, SPECIAL OR CONSEQUENTIAL DAMAGES, COSTS, EXPENSES, LEGAL FEES, OR LOSSES (INCLUDING LOST INCOME OR PROFITS AND OPPORTUNITY COSTS OR LOSSES CAUSED BY NEGLIGENCE) IN CONNECTION WITH ANY USE OF THEIR INFORMATION OR CONTENT, INCLUDING RATINGS. Credit ratings are statements of opinions and are not statements of fact or recommendations to purchase, hold or sell securities. They do not address the suitability of securities or the suitability of securities for investment purposes, and should not be relied on as investment advice."

Certain information in this report may be provided by Securities Evaluations, Inc. ("SE"), a wholly owned subsidiary of Intercontinental Exchange. SE is a registered investment adviser with the United States Securities and Exchange Commission (SEC). SE's advisory services include evaluated pricing and model valuation of fixed income securities, derivative valuations and Odd-Lot Pricing that consists of bid- and ask-side evaluated prices for U.S. Municipal and U.S. Corporate Securities (together called valuation services). Such information is subject to the following disclaimers and notices: "No content (including credit-related analyses and data, valuations, model, software or other application or output therefrom) or any part thereof (Content) may be modified, reverse engineered, reproduced or distributed in any form by any means, or stored in a database or retrieval system, without the prior written permission of SE. The Content shall not be used for any unlawful or unauthorized purposes. SE and any third-party providers, as well as their directors, officers, shareholders, employees or agents (collectively SE Parties) do not guarantee the accuracy, completeness, timeliness or availability of the Content. SE Parties are not responsible for any errors or omissions (negligent or otherwise), regardless of the cause, for the results obtained from the use of the Content, or for the security or maintenance of any data input by the user. The Content is provided on an "as is" basis. SE PARTIES DISCLAIM ANY AND ALL EXPRESS OR IMPLIED WARRANTIES, INCLUDING, BUT NOT LIMITED TO, ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR USE, FREEDOM FROM BUGS, SOFTWARE ERRORS OR DEFECTS, THAT THE CONTENT'S FUNCTIONING WILL BE UNINTERRUPTED OR THAT THE CONTENT WILL OPERATE WITH ANY SOFTWARE OR HARDWARE CONFIGURATION.

In no event shall SE Parties be liable to any party for any direct, indirect, incidental, exemplary, compensatory, punitive, special or consequential damages, costs, expenses, legal fees, or losses (including, without limitation, lost income or lost profits and opportunity costs or losses caused by negligence) in connection with any use of the Content even if advised of the possibility of such damages. Credit-related and other analyses and statements in the Content are statements of opinion as of the date they are expressed and not statements of fact or recommendations to purchase, hold, or sell any securities or to make any investment decisions. SE assumes no obligation to update the Content following publication in any form or format. The Content should not be relied on and is not a substitute for the skill, judgment and experience of the user, its management, employees, advisors and/or clients when making investment and other business decisions. SE's opinions and analyses do not address the suitability of any security. SE does not act as a fiduciary or an investment advisor. While SE has obtained information from sources it believes to be reliable, SE does not perform an audit and undertakes no duty of due diligence or independent verification of any information it receives. Valuations services are opinions and not statements of fact or recommendations to purchase, hold or sell any security or instrument, or to make any investment decisions. The information provided as part of valuations services should not be intended as an offer, promotion or solicitation for the purchase or sale of any security or other financial instrument nor should it be considered investment advice. Valuations services do not address the suitability of any security or instrument, and securities, financial instruments or strategies mentioned by SE may not be suitable for all investors. SE does not provide legal, accounting or tax advice, and clients and potential clients of valuation services should consult with an attorney and/or a tax or accounting professional regarding any specific legal, tax or accounting provision(s) applicable to their particular situations and in the countries and jurisdictions where they do business. SE has redistribution relationships that reflect evaluated pricing, derivative valuation and/or equity pricing services of other unaffiliated firms with which SE has contracted to distribute to its client base. Pricing and data provided by these third-party firms are the responsibilities of those firms, and not SE, and are produced under those firms' methodologies, policies and procedures. Valuations services provided by SE and products containing valuations services may not be available in all countries or jurisdictions. Copyright © 2022 by Intercontinental Exchange Inc. All rights reserved."

Redistribution or reproduction is prohibited without written permission. Copyright © 2022 CFRA. All rights reserved.