Author:

Ryan O. Issakainen, CFA
Senior Vice President
Exchange-Traded Fund Strategist
First Trust Advisors L.P.

Co-author:

Andrew Hull
Vice President
Exchange-Traded Fund Strategist
First Trust Advisors L.P.

Hopeful Signs Emerging for the Biotechnology Industry

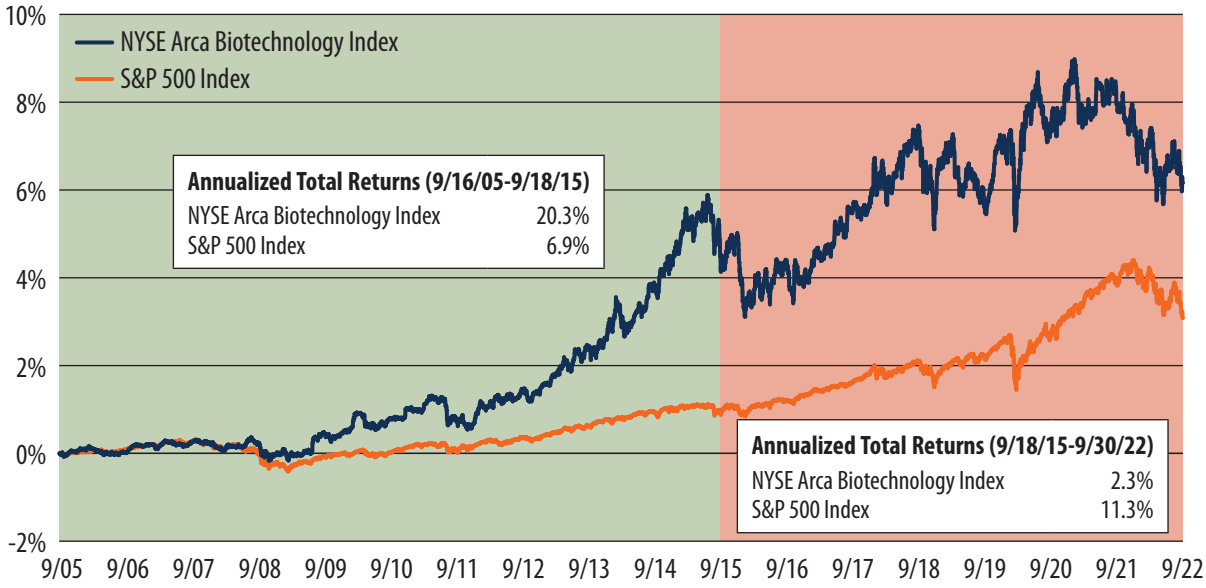
The biotechnology and pharmaceutical industries have positively impacted the lives of billions of people over the past few years with the rapid development of therapeutics and vaccines for Covid-19. However, the biotechnology industry, which is generally credited with driving the most cutting-edge innovation, has underperformed the broader stock market over the past few years. Performance aside, hopeful signs are emerging thanks to more clarity on which drugs may be impacted by future anticipated price controls stemming from the recent passage of the Inflation Reduction Act, a robust pipeline of promising medicines and therapeutics, and a surprisingly resilient track record for the industry during periods of economic weakness. In our view, biotechnology is uniquely positioned to provide exposure to important innovations whose value may not be well reflected in equity prices today.

The Silver Lining to Price Controls

Health care costs have been a wedge issue for voters for many years, and the biotechnology industry has been an easy target for politicians across the political spectrum. To bring a new drug to market costs companies an average of $2.6 billion and a 10-15 year commitment taking it from inception through various stages of clinical testing.[1] Keep in mind, once a new drug is invented, any patents issued are good for 20 years. To recoup these outlays and earn a profit, drug companies may charge thousands of dollars for certain medicines, often causing "sticker shock" when prices are publicized. While history has shown that price controls rarely work as intended, often creating shortages and disincentives for investment, politicians sometimes find the temptation to propose such measures irresistible. Such has been the situation over much of the past six years.

During the 2016 U.S. presidential election, prominent candidates from both major political parties announced their support for policies to effectively cap the price of some prescription drugs. In September of 2015, Democratic candidate Hillary Clinton sent a tweet announcing her plan to take on "price gouging" in the specialty drug market. This threat took many investors by surprise, and the NYSE Arca Biotechnology Index declined by 16% over the next month (the S&P 500 index was up 3%).[2] A few months later, Republican candidate Donald Trump gave a speech during which he embraced the idea that Medicare should "negotiate" drug prices with pharmaceutical companies. Over the next two weeks, the NYSE Arca Biotechnology Index declined by nearly 16% (the S&P 500 Index was down 1%).[3] A desire to enact price controls on prescription drugs seemed to be one of the few areas that had bipartisan agreement, even as little was done legislatively during the Trump administration or the first couple years of the Biden administration.

Cumulative Returns (9/16/2005-9/30/2022)



Source: Bloomberg. For illustrative purposes only and not indicative of any actual investment. **Past performance is no guarantee of future results.**

While there have been many factors that have impacted the performance of biotechnology stocks since the 2016 presidential campaign, we believe an ambiguous, looming threat of potential price controls has been a key drag on performance and investor sentiment. Over the decade that preceded Hillary Clinton's initial tweet, the NYSE Arca Biotechnology Index had an average annual return of 20.3% compared with 6.9% for the S&P 500 Index (see chart above).[4] Since then, average annual returns for the NYSE Arca Biotechnology Index have been 2.3%, compared to 11.3% for the S&P 500 Index.[5]

[1]PhRMA, "Innovation in the Biopharmaceutical Pipeline". December 2021.

[2]Clinton tweet was sent in the morning of 9/21/15; performance cited is 9/18/15-10/21/15.

[3]Trump speech was given on 1/25/16; performance cited is 1/25/16-2/8/16.

[4]9/16/05-9/18/15.

[5]9/18/15-9/30/22.

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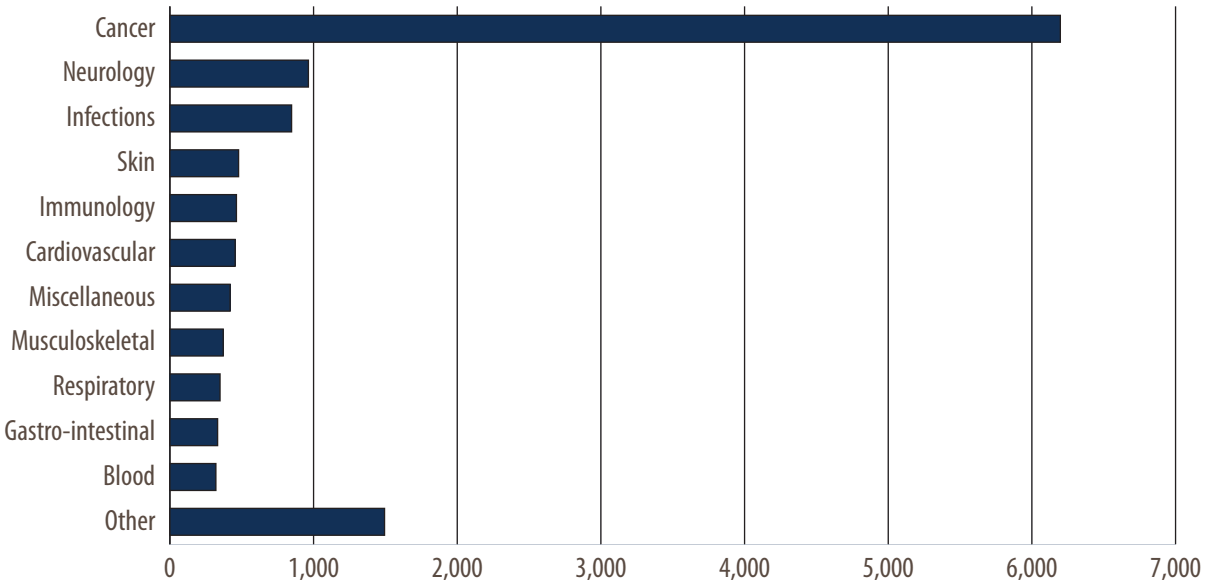
As previously noted, the issue of price controls finally reached some resolution with the passage of the Inflation Reduction Act in August, which included provisions to effectively cap prices on certain drugs in the future. For example, beginning in 2026, the new law compels drug companies to offer "negotiated" prices to Medicare on certain top-selling drugs that don't have generic equivalents and have been FDA-approved for at least nine years (or 13 years for biologics). While such requirements may negatively impact the expected profitability of those drugs—and may also have unintended consequences as companies seek to preserve profits—we think a silver lining of the new law is that it defines the scope and timing of which drugs may be impacted. In effect, this also helps to define which drugs won't be impacted by price controls. In our view, this may improve investor sentiment by diminishing this perceived risk.

Innovation is Flourishing

Innovation is flourishing in the biotechnology industry as companies race to develop treatments for devastating diseases that impact millions of patients each year. As of January 2021, the biotech and pharmaceutical industries had roughly 12,700 projects filed with the FDA, a 33% increase from five years earlier.[6] Among these, cancer was the most frequently targeted disease, representing nearly half of all projects, followed by neurology (i.e., Alzheimer's Disease, Parkinson's Disease, ALS, etc.) and infectious diseases (see breakdown in chart below). Almost 70% of these projects are for potentially first-in-class medicines that represent a new pharmacological class or mechanism of action.[7]

Chart 2: Total Clinical Phase Projects



Source: PhRMA, "Innovation in the Biopharmaceutical Pipeline". December 2021.

In addition to small molecule medicines, which have long been the primary modality for drug development, new therapeutic technologies represent a growing number of projects in clinical development. As of January 2021, there were 2,533 projects using monoclonal antibodies or conjugated monoclonal antibodies, 1,174 projects using gene-, cell-, or gene-modified cell therapy, and 265 projects using DNA or RNA therapeutics.[8]

Much of the innovation occurring in biotechnology has been facilitated by other technological advances, such as cloud computing and artificial intelligence, which have enabled researchers to analyze and interpret massive amounts of data. These tools have helped to solve exceptionally complex problems that hinder drug development. For example—in what has been hailed as the most important achievement in artificial intelligence so far—an AI platform known as AlphaFold has been utilized to predict the structure of nearly all the 214 million proteins currently known to science.[9] This is a huge leap forward for researchers that previously required multi-million-dollar equipment and several months of laboratory experiments to understand a protein's structure, which can be critical for drug development. While such breakthroughs don't necessarily create any new medicines on their own, technology is radically improving efficiency and accelerating innovation by alleviating key pain points in drug development.

[6-8]PhRMA, *"Innovation in the Biopharmaceutical Pipeline".* December 2021.

[9]Wall Street Journal, *DeepMind AI Lab Predicts Structure of Most Proteins,* 7/28/22.

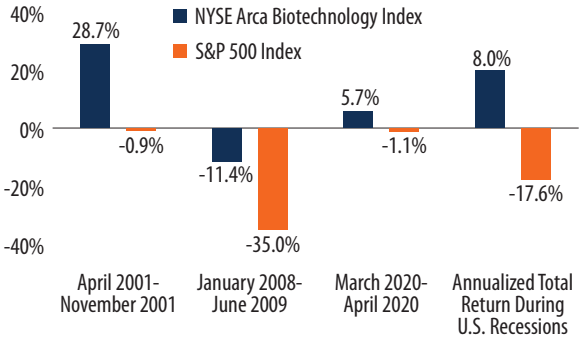
Is Biotechnology Defensive?

Health care is often viewed as a "defensive" sector because demand for drugs and other medical care is generally just as strong during economic recessions as it is during expansions. Many health care companies may also have pricing power during periods of high inflation since demand tends to be relatively inelastic. While the biotechnology industry is generally regarded as a riskier segment of the health care sector, it too has tended to perform relatively well amid economic weakness. In fact, the NYSE Arca Biotechnology Index outperformed the S&P 500 in each of the last three economic recessions, producing an 8.0% annualized total return, compared to -17.6% for the S&P 500 (see chart below).

Chart 3A: Cumulative Returns (12/29/00 - 9/30/22)

Source: Bloomberg. For illustrative purposes only and not indicative of any actual investment. **Past performance is no guarantee of future results.**

Chart 3B: Returns During Recent U.S. Recessions



Investors should take such a small sample size with a grain of salt (only three recessions), but we believe certain factors that led to biotechnology's outperformance in past recessions may also be relevant today. For example, during the "great recession" that stretched from January of 2008 until June of 2009, the NYSE Arca Biotechnology Index declined by less than 12%, while the S&P 500 Index declined by 35%. A significant portion of this outperformance followed announcements by constituent stocks related to positive drug trial results or M&A activity. In July of 2008 alone, the NYSE Arca Biotechnology Index advanced by over 17% following announcements related to both, while the S&P 500 Index declined almost 1%.[10] In our opinion, investors have great difficulty forecasting the probability of such events, so they are seldom (fully) incorporated into stock prices. Scientific breakthroughs, positive trial results, favorable regulatory decisions, and M&A activity can occur during any phase of the economic cycle, including recessions. In our view, these key factors help to explain why the biotechnology industry's returns have been less correlated to other sectors of the economy.

Encouraging Signs for Biotechnology

The biotechnology industry faced a tough stretch over the past few years, but we see encouraging signs unfolding. Although drug pricing policies found in the Inflation Reduction Act may negatively impact certain companies in the future, they also clarify which drugs are less likely to face price caps, which may improve investor sentiment, in our opinion. Meanwhile, technology is helping to facilitate a wave of innovation, as biotechnology researchers pursue cures and treatments for a host of terrible diseases. Lastly, we believe the biotechnology industry may contribute a unique set of characteristics to an investor's overall portfolio allocation, as many of the factors that drive its performance are both difficult to handicap and unrelated to the economic cycle.

[10]Eli Lilly announced an acquisition of Imclone; Amgen announced positive phase 3 trial results for an osteoporosis drug.