Biotechnology: A Potential Cure for Economic Uncertainty

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The long-term secular growth story for biotechnology stocks is compelling, in our opinion. Over the next several decades, an aging global population will support massive demand for cures and treatments for a variety of diseases, especially those associated with old age. At the same time, innovation is flourishing for biotechnology companies racing to meet these needs, supported by new technologies such as artificial intelligence/machine learning, which enables researchers to analyze massive amounts of data more efficiently, or cloud-based infrastructure, which provides virtually unlimited computing power.

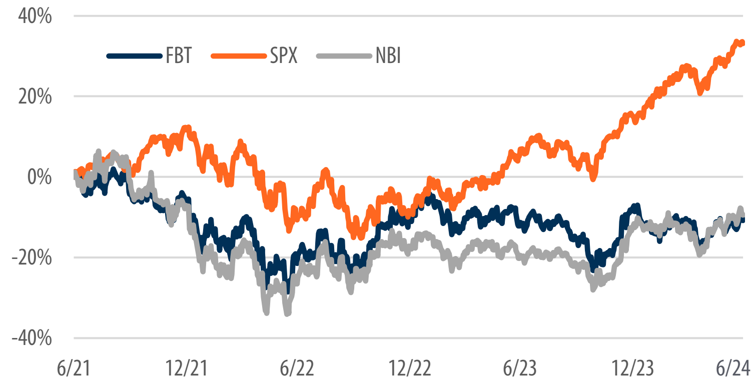
Over much of the past few years, biotechnology stocks have struggled with a hangover from COVID-19, higher costs of capital, and political pressure related to drug pricing. For the three-year period ending on June 30, 2024, the First Trust NYSE® Arca® Biotechnology Index Fund (FBT) produced a cumulative loss of 10.9%, compared to a 33.1% gain for the S&P 500® Index. However, over the past several weeks, momentum has begun to shift in favor of the biotechnology industry. Since June 30, 2024, FBT has posted an 11.1% total return, compared to a 6.8% gain for the Nasdaq Biotechnology™ Index and a 2.7% gain for the S&P 500® Index (as of 8/20/24). Below we discuss a few potential catalysts that may continue to benefit biotechnology stocks in the months ahead, in our opinion, including falling interest rates, increased mergers and acquisitions ("M&A") activity, and rising demand for defensive sectors if the economy slows.

Biotechnology and Interest Rates

Interest rates have had a meaningful impact on biotechnology stock prices over the past couple years. Rising interest rates have generally been a headwind for biotechnology stocks and falling interest rates have been a tailwind (see charts 3 and 4 below). Since the end of 2022, the correlation between FBT and the 10-year U.S. Treasury yield was -0.37.[1]

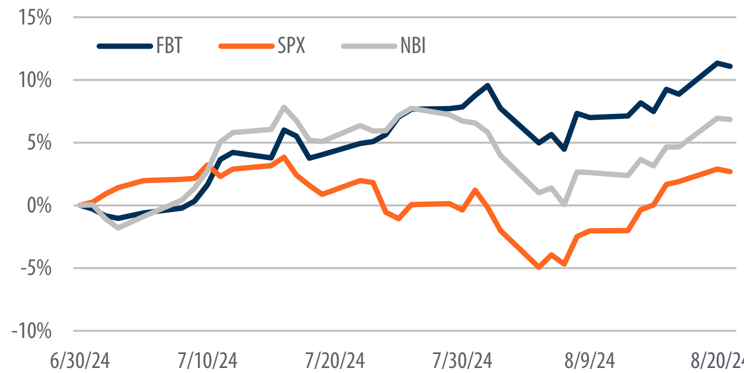
Drug development is a challenging business with a low success rate. To bring a new drug to market, companies spend an average of $2.6 billion and commit 10-15 years to rigorous clinical testing.[2] Historically, only one of 10,000-15,000 investigated compounds make it to the finish line.[3] Many biotech companies do not have any marketed products and are cash flow negative, making them reliant on capital markets and larger pharmaceutical companies to fund development. As interest rates and the cost of capital rise, the hurdle rate for funding lower probability projects increases as capital becomes scarcer. Conversely, if rates continue to trend lower over the next couple years, we believe biotechnology companies may benefit as capital begins to flow toward riskier projects.

Chart 1: Cumulative Total Return (June 2021 – June 2024)



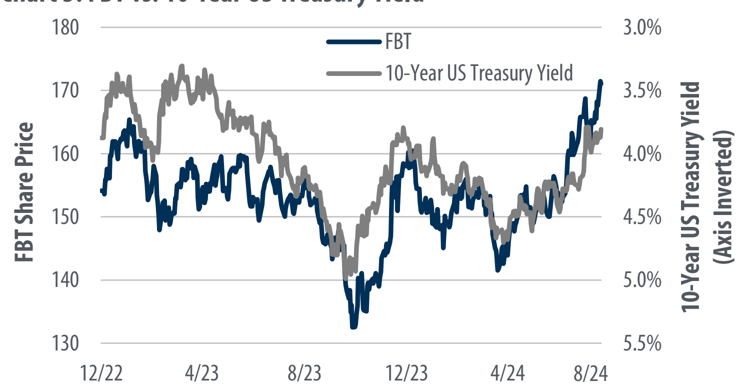
Source: Bloomberg. Data from 6/30/21 - 6/28/24.

Chart 2: Cumulative Total Return (June 2024 – August 2024)



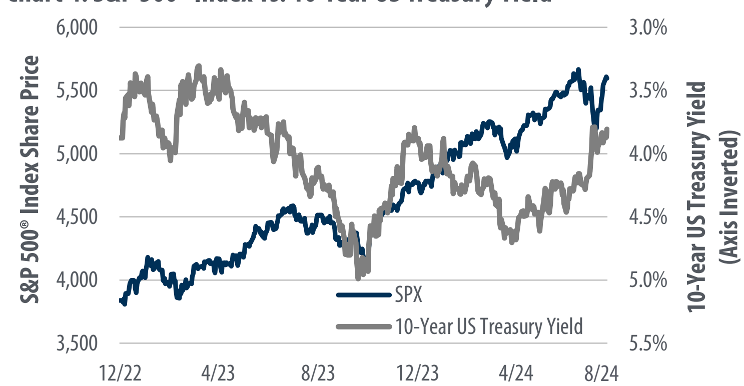
Source: Bloomberg. Data from 6/30/24 - 8/20/24.

Chart 3: FBT vs. 10-Year US Treasury Yield



Source: Bloomberg. Data from 12/30/22-8/20/24.

Chart 4: S&P 500® Index vs. 10-Year US Treasury Yield



Source: Bloomberg. Data from 12/30/22-8/20/24.

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Performance information for each index shown in the charts is for illustrative purposes only and does not represent actual fund performance. Indexes do not charge management fees or brokerage expenses, and no such fees or expenses were deducted from the performance shown. Indexes are unmanaged and an investor cannot invest directly in an index.

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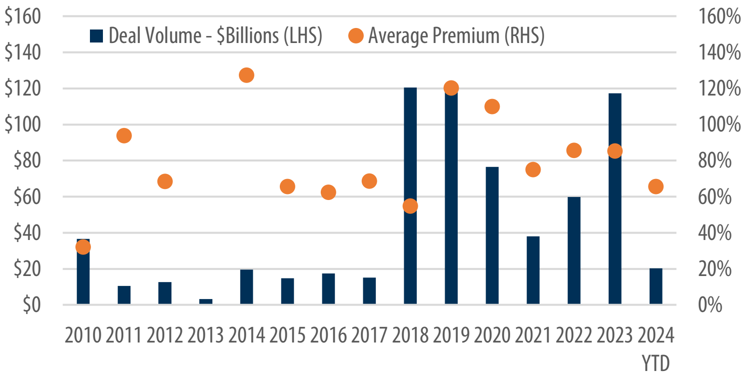
Lower Rates Could Mean More M&A

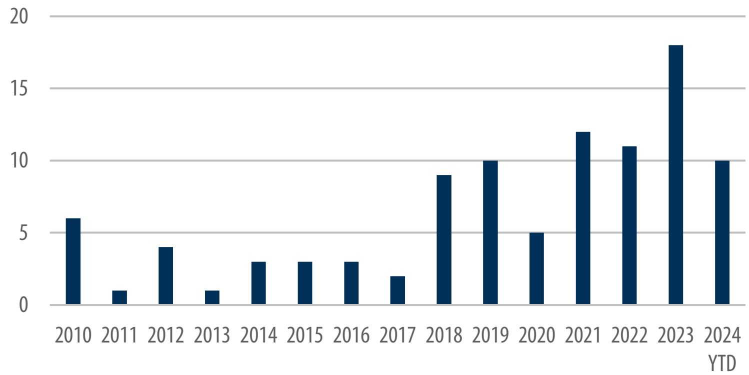
In our opinion, lower interest rates may also increase M&A activity as large pharmaceutical companies focus on replenishing their drug-development pipelines. M&A activity has historically been an important contributor to the returns of biotechnology stocks. Over the past decade, the average premium paid for an acquired biotech stock has been roughly 80%.[4] Though the total dollar volume of deals remains below levels seen recently, the number of deals exceeding $1 billion has been robust following COVID-19. In addition to lower interest rates, we believe a combination of government-related price pressures and looming patent cliffs provide strong incentives for increased M&A activity over the next few years.[5]

Chart 5: Biotech Deal Volume



Source: Bloomberg. Data from 12/31/10 - 8/12/24.

Chart 6: Deal Count Greater than $1 Billion



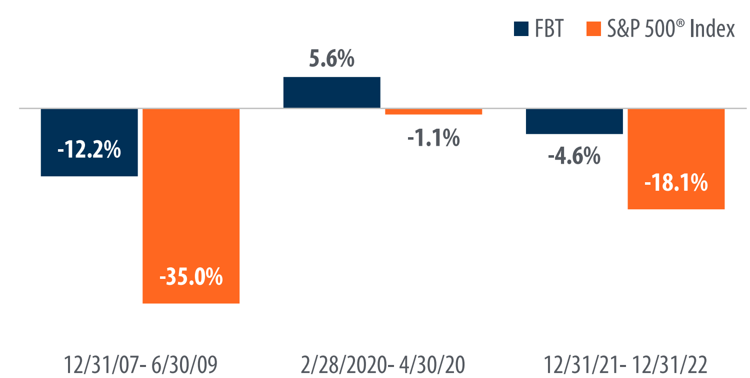
Source: Bloomberg. Data from 12/31/10 - 8/12/24.

Playing Defense

The health care sector has historically provided exposure to defensive, non-cyclical growth due to the non-discretionary nature of health care spending and global demographic tailwinds. While biotechnology tends to be more volatile than other industries within the health care sector, the potential for new drug discovery and cutting-edge therapies provides exposure to growth that is less dependent on economic cycles. Factors such as scientific breakthroughs, the timing of clinical trials results, and regulatory approvals are unique drivers that can impact biotech returns in various economic environments. Consequently, returns for biotechnology stocks have historically been less correlated to broad market indices than many other sectors. Over the past decade, the correlation of FBT to the S&P 500® Index was 0.61, meaningfully lower than the Information Technology sector (+0.90), the Industrials sector (+0.91), and even the broader Health Care sector (+0.80).[6]

FBT has also tended to perform surprisingly well during economic recessions and other periods of market stress. For example, FBT significantly outperformed the S&P 500® Index during the recessionary periods from January 2008-June 2009 and March 2020-April 2020. More recently, FBT outperformed the S&P 500® Index in 2022, as the U.S. economy avoided a recession, but had two consecutive quarters of negative GDP growth (see chart above).

Chart 7: FBT vs. S&P 500® Index



Source: Bloomberg. Data from 12/31/2007-12/31/2022.

A Difference Approach

FBT provides a differentiated approach for investors seeking exposure to the dynamic potential of the biotechnology industry. This ETF invests in an equal-weight portfolio of 30 biotechnology stocks that have been selected based on several factors including:

- Net sales (revenue) over the last 12 months
- Ratio of net sales to research & development ("R&D") expenditures over the last 12 months
- Percentage change in R&D expenditures over the last 12 months compared to three years prior

By screening for net sales, FBT eliminates stocks that are pre-revenue, while focusing instead on those with a demonstrated ability to bring a product to market. A biotech stock's ratio of net sales to R&D expenditures may be helpful for identifying companies that have efficiently monetized R&D spending. And companies that have grown R&D expenditures over the past few years may be better positioned for introducing future innovations. Each quarter, the stock selection process is reapplied, and the portfolio is rebalanced.

Over the near-term, we believe catalysts are emerging for biotechnology stocks, including lower interest rates, the potential for increased M&A activity, and rising demand for defensive growth. As the global population ages and scientific understanding is accelerated by the application of new technologies, we believe FBT offers a compelling long-term investment opportunity.

Performance data quoted represents past performance. Past performance is not a guarantee of future results and current performance may be higher or lower than performance quoted. Investment returns and principal value will fluctuate and shares when sold or redeemed, may be worth more or less than their original cost. You can obtain performance information which is current through the most recent month-end by visiting www.ftportfolios.com.

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Performance Summary (%) as of 6/28/24

FBT Performance*	3 Month	YTD	1 Year	3 Year	5 Year	10 Year	Since Fund Inception
Net Asset Value (NAV)	-0.02	-2.58	0.87	-3.76	1.80	6.48	12.07
Market Price	0.00	-2.51	0.81	-3.74	1.81	6.48	12.07
Index Performance**							
NYSE® Arca® Biotechnology Index	0.12	-2.31	1.44	-3.35	2.29	6.98	12.65
Nasdaq Biotechnology™ Index	2.85	4.47	12.43	-3.28	6.59	6.01	11.22
S&P Composite 1500® Health Care Index	-1.07	7.48	10.85	5.75	11.05	11.04	11.33
S&P 500® Index	4.28	15.29	24.56	10.01	15.05	12.86	10.74

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*__NAV__ returns are based on the fund's net asset value which represents the fund's net assets (assets less liabilities) divided by the fund's outstanding shares. **Market Price** returns are determined by using the midpoint of the national best bid offer price ("NBBO") as of the time that the fund's NAV is calculated. Returns are average annualized total returns, except those for periods of less than one year, which are cumulative. The fund's performance reflects fee waivers and expense reimbursements, absent which performance would have been lower.

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The gross expense ratio for this fund is 0.56%. The net expense ratio for this fund is 0.56%. Expenses are capped contractually at 0.60% per year, at least through April 30, 2025. Fund Inception Date: 6/19/2006.

[1] Bloomberg. Correlation of weekly returns from 12/31/22-8/16/24.

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

[3] ThermoFisher Scientific.

[4] Bloomberg, data includes M&A deals targeting publicly-traded biotechnology companies with market capitalizations greater than $1 billion, over a 10-year period ending on 7/31/2024.

[5] Drug Discovery & Development, April 2023.

[6] Bloomberg, Correlation of monthly returns over 10 years ending on 7/31/2024.

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You should consider a fund's investment objectives, risks, and charges and expenses carefully before investing. Contact First Trust Portfolios L.P. at 1-800-621-1675 or visit www.ftportfolios.com to obtain a prospectus or summary prospectus which contains this and other information about a fund. The prospectus or summary prospectus should be read carefully before investing.

RISK CONSIDERATIONS

You could lose money by investing in a fund. An investment in a fund is not a deposit of a bank and is not insured or guaranteed. There can be no assurance that a fund's objective(s) will be achieved. Investors buying or selling shares on the secondary market may incur customary brokerage commissions. Please refer to each fund's prospectus and Statement of Additional Information for additional details on a fund's risks. The order of the below risk factors does not indicate the significance of any particular risk factor.

Unlike mutual funds, shares of the fund may only be redeemed directly from a fund by authorized participants in very large creation/redemption units. If a fund's authorized participants are unable to proceed with creation/redemption orders and no other authorized participant is able to step forward to create or redeem, fund shares may trade at a premium or discount to a fund's net asset value and possibly face delisting and the bid/ask spread may widen.

Biotechnology and pharmaceutical companies are subject to changing government regulation which could have a negative effect on the price, profitability and availability of their products and services. Biotechnology and pharmaceutical companies face increasing competition from generic drugs, termination of their patent protection and technological advances which render their products or services obsolete. The research and development costs required to bring a drug to market are substantial and may include a lengthy review by the government, with no guarantee that the product will ever be brought to market or show a profit. Many of these companies may not offer certain drugs or products for several years, and as a result, may have significant losses of revenue and earnings.

Current market conditions risk is the risk that a particular investment, or shares of the fund in general, may fall in value due to current market conditions. As a means to fight inflation, the Federal Reserve and certain foreign central banks have raised interest rates and expect to continue to do so, and the Federal Reserve has announced that it intends to reverse previously implemented quantitative easing. Recent and potential future bank failures could result in disruption to the broader banking industry or markets generally and reduce confidence in financial institutions and the economy as a whole, which may also heighten market volatility and reduce liquidity. Ongoing armed conflicts between Russia and Ukraine in Europe and among Israel, Hamas and other militant groups in the Middle East, have caused and could continue to cause significant market disruptions and volatility within the markets in Russia, Europe, the Middle East and the United States. The hostilities and sanctions resulting from those hostilities have and could continue to have a significant impact on certain fund investments as well as fund performance and liquidity. The COVID-19 global pandemic, or any future public health crisis, and the ensuing policies enacted by governments and central banks have caused and may continue to cause significant volatility and uncertainty in global financial markets, negatively impacting global growth prospects.

A fund is susceptible to operational risks through breaches in cyber security. Such events could cause a fund to incur regulatory penalties, reputational damage, additional compliance costs associated with corrective measures and/or financial loss.

Depositary receipts may be less liquid than the underlying shares in their primary trading market and distributions may be subject to a fee. Holders may have limited voting rights, and investment restrictions in certain countries may adversely impact their value.

Equity securities may decline significantly in price over short or extended periods of time, and such declines may occur in the equity market as a whole, or they may occur in only a particular country, company, industry or sector of the market.

Health care companies may be affected by government regulations and government health care programs, increases or decreases in the cost of medical products and services and product liability claims, among other factors. Many health care companies are heavily dependent on patent protection, and the expiration of a company's patent may adversely affect that company's profitability. Health care companies are also subject to competitive forces that may result in price discounting, may be thinly capitalized and susceptible to product obsolescence.

An index fund will be concentrated in an industry or a group of industries to the extent that the index is so concentrated. A fund with significant exposure to a single asset class, or the securities of issuers within the same country, state, region, industry, or sector may have its value more affected by an adverse economic, business or political development than a broadly diversified fund.

A fund may be a constituent of one or more indices or models which could greatly affect a fund's trading activity, size and volatility.

There is no assurance that the index provider or its agents will compile or maintain the index accurately. Losses or costs associated with any index provider errors generally will be borne by a fund and its shareholders.

Large capitalization companies may grow at a slower rate than the overall market.

Market risk is the risk that a particular security, or shares of a fund in general may fall in value. Securities are subject to market fluctuations caused by such factors as general economic conditions, political events, regulatory or market developments, changes in interest rates and perceived trends in securities prices. Shares of a fund could decline in value or underperform other investments as a result. In addition, local, regional or global events such as war, acts of terrorism, spread of infectious disease or other public health issues, recessions, natural disasters or other events could have significant negative impact on a fund.

A fund faces numerous market trading risks, including the potential lack of an active market for fund shares due to a limited number of market makers. Decisions by market makers or authorized participants to reduce their role or step away in times of market stress could inhibit the effectiveness of the arbitrage process in maintaining the relationship between the underlying values of a fund's portfolio securities and a fund's market price.

An index fund's return may not match the return of the index for a number of reasons including operating expenses, costs of buying and selling securities to reflect changes in the index, and the fact that a fund's portfolio holdings may not exactly replicate the index.

Securities of non-U.S. issuers are subject to additional risks, including currency fluctuations, political risks, withholding, lack of liquidity, lack of adequate financial information, and exchange control restrictions impacting non-U.S. issuers.

A fund and a fund's advisor may seek to reduce various operational risks through controls and procedures, but it is not possible to completely protect against such risks. The fund also relies on third parties for a range of services, including custody, and any delay or failure related to those services may affect the fund's ability to meet its objective.

A fund that invests in securities included in or representative of an index will hold those securities regardless of investment merit and the fund generally will not take defensive positions in declining markets.

Pharmaceutical companies are subject to changing government regulation which could have a negative effect on the price, profitability and availability of their products and services. Regulations have been proposed to increase the availability and affordability of prescription drugs including proposals to increase access to generic drugs and to increase the rebates paid by drug manufacturers in exchange for Medicaid coverage of their products. Whether such proposals will be adopted cannot be predicted. In addition, such companies face increasing competition from existing generic drugs, the termination of their patent protection for certain drugs and technological advances which render their products or services obsolete. The research and development costs required to bring a drug to market are substantial and may include a lengthy review by the government, with no guarantee that the product will ever be brought to market or show a profit. In addition, the potential for an increased amount of required disclosure of proprietary scientific information could negatively impact the competitive position of these companies. Many of these companies may not offer certain drugs or products for several years, and as a result, may have significant losses of revenue and earnings.

High portfolio turnover may result in higher levels of transaction costs and may generate greater tax liabilities for shareholders.

The market price of a fund's shares will generally fluctuate in accordance with changes in the fund's net asset value ("NAV") as well as the relative supply of and demand for shares on the exchange, and a fund's investment advisor cannot predict whether shares will trade below, at or above their NAV.

Securities of small- and mid-capitalization companies may experience greater price volatility and be less liquid than larger, more established companies.

Trading on an exchange may be halted due to market conditions or other reasons. There can be no assurance that a fund's requirements to maintain the exchange listing will continue to be met or be unchanged.

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DEFINITIONS

Nasdaq Biotechnology™ Index includes securities of NASDAQ-listed companies classified as either Biotechnology or Pharmaceuticals which also meet other eligibility criteria.

S&P Composite 1500® Health Care Index is a capitalization-weighted index of companies classified by GICS as health care within the S&P Composite 1500 Index.

S&P 500® Index is an unmanaged index of 500 companies used to measure large-cap U.S. stock market performance.