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The Oncology ETF: How Retail Traders Can Utilize Custom Growth ETF’s

Samuel Sprute
ssprute@lion.lmu.edu

Loyola Marymount University
University Honors Program

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Samuel Sprute

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Samuel Sprute, Mentor: Dr. Dennis Draper

Abstract

Exchange Traded Funds (ETFs) are potent investment vehicles to generate returns from systematic gains in any market. However, they have historically been products created and distributed by large financial institutions. Due to various drawbacks of institutionally available ETFs, many retail traders have begun to create their own custom ETFs. These custom ETFs operate as mini-portfolios and have significant potential to generate alpha, or positive risk-adjusted return, when positioned specifically in growth markets.

In this work I aim to show the potential for custom ETFs in retail trading. In achieving this goal, I have broken this work into two sections. The first section will give a history of ETFs and explain the various ETF investment strategies. The second section will then be a case study detailing the process of creating a custom ETF for the oncology pharmaceuticals industry. In this section I will first give a brief overview of the oncology economy to explain why it is an ideal candidate for a custom ETF. I will then detail the process of creating said custom ETF, including search tactics, inclusion principles, a case study of a high potential passed security, and how I determined portfolio weightings by optimizing the projected portfolio Sharpe ratio.

Part 1: The ETF Renaissance

The Origin of ETF's

ETFs, or Exchange-Traded Funds, are hybrid investment products which combine the "investment features of mutual funds" with the "trading features of common stocks."[1] ETFs generally follow the index investing strategy. Index investing is a passive investing strategy seeking to replicate the returns of a benchmark index. The first public index mutual fund, the Vanguard 500 Index Fund, was created in 1975. Despite great success, index mutual funds still had one large drawback: liquidity. To invest in a mutual fund, an investor must buy and redeem their shares directly with the fund or a brokerage that sells the fund. While it is easy enough to do this on a daily basis, it was still not as quick or efficient as trading assets on an actual exchange. So, in the 1990s ETFs were created and brought with them intra-day liquidity and continuous pricing. The S&P 500 was the first ETF available in the US. Beginning from this foundation of stock index replication, ETFs began experimentally expanding offerings in the 2000s. Now, there are ETFs focused on specific countries, sectors, and sub-industries that are based on various commodities such as fixed-income and currency ETFs. [2] Although this study focuses exclusively on stock-based ETFs, their broad usage across various investment focuses should be noted. As ETF focuses began expanding, so did the number of ETFs available. They are one of the fastest growing asset classes of the 21st century with an average of 446 new ETFs introduced every year between 2003 and 2022.

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[1] Hill, Joanne M., Dave Nadig, and Matt Hougan. *A comprehensive guide to exchange-traded funds (ETFs)*. CFA Institute Research Foundation, 2015.

[2] Deville, Laurent. "Exchange traded funds: History, trading, and research." *Handbook of financial engineering*. Boston, MA: Springer US, 2008. 67-98.

Figure1: ETFs publicly available and traded 2003-2022.

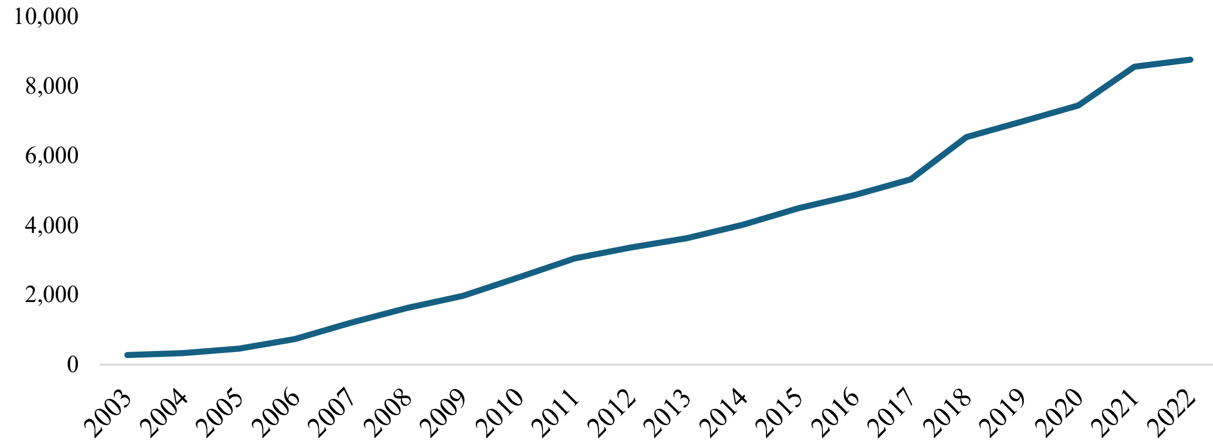

Figure 1: The graph above depicts the increase in ETFs publicly traded. These ETFs are diversified across asset base, region, risk profile, management, and more. ETFs are now one of the largest asset classes in the world.[3]

ETF Investing Strategies

ETFs generally utilize passive investing strategies. Passive investing, as opposed to active investing, involves the holding of a security for a prolonged period. Research into passive investing began as early as the 1940s with Benjamin Graham. Graham is widely considered the father of value investing, and through his seminal works *Security Analysis* and *The Intelligent Investor* began drawing significant attention from institutional and retail traders alike to the vast potential of value investing. Value investing is closely linked to passive investing as both rely on the assumption that a security has some intrinsic value. This intrinsic value is either accurately or inaccurately reflected by the market. When there is disparity between a company's intrinsic value and its current market pricing, an investor can opportunistically invest in it and hold until market sentiment corrects to reflect the true value of the company. Thus, value investing is the methodology of identifying mispriced assets and passive investing is the strategy employed to hold until there is proper market pricing. In the case of ETFs, they take advantage of broad

[3] Deutsche Bank, and ETFGI. "Number of Exchange Traded Funds (Etfs) Worldwide from 2003 to 2022." *Statista*, Statista Inc., 2 Feb 2023, https://www.statista.com/statistics/278249/global-number-of-etfs/

market exposure to generate returns from cumulative increases to intrinsic value as well as corrections on securities which were undervalued at the time of investment in the ETF.

Some ETFs, however, do not utilize passive investing strategies and are actively managed by the institutions that created them. Active investing attempts to generate returns in excess of the general market by forecasting pricing movements and increasing or decreasing specific holdings to take advantage of the security's volatility. However, many active investors quickly decrease portfolio returns by acting on poor forecasting. Fellow LMU Honors Alumni Zachary Bishkin researched this in his senior thesis "Evaluating Morningstar Wide Moat Stocks through the Business Cycle." Bishkin found that a portfolio actively managed by Morningstar investment professional fell short of generating alpha, or risk-adjusted returns in excess of the general market. Alpha is tricky to achieve due to the fact that even if returns exceed the general market, if the risk profile also exceeds the general market, you can have lower risk-adjusted returns. Furthermore, Bishkin found the Wide Moat strategy utilized by Morningstar investment professional relied more on industry competitiveness and a retail trader could mimic this portfolio's returns by "invest[ing] in an ETF that focuses on large market cap corporations that hold large market share."[4] Prondzinski and Miller had similar findings in their 2018 publishing *Active versus passive investing: Evidence from the 2009-2017 market*. Prondzinski and Miller showed that passive indices had higher mean daily sharpe ratios.[5] This means that, on average, passive indices created better risk-adjusted return compared to active asset management. Passive investing and active investing can both claim to be based on value investing principals; however, due to the random walk phenomenon generally seen in short-term security returns, actively

[4] Bishkin, Zachary, "Evaluating Morningstar Wide Moat Stocks through the Business Cycle" (2019). *Honors Thesis*. 182. https://digitalcommons.lmu.edu/honors-thesis/182

[5] Prondzinski, Dale, and Mitchell Miller. "Active versus passive investing: Evidence from the 2009-2017 market." *Journal of Accounting and Finance* 18.8 (2018): 119-143.

investing can quickly dilute overall returns by acting on poor forecasting.[6] While active management does have its place in creating and maintaining a portfolio, it is generally better to rely on fundamentals and time in the market than attempting to time the market.

Another strategy to creating and managing ETFs is the Smart-Beta (SB) approach. While traditional ETFs are typically market cap weighted, price weighted, or equal weighted, SB ETFs utilize a rules-based approach to choose stocks and allocate an appropriate weighting to them. They might pick companies that have specific behaviors or metrics in order to build on traditional indexing strategies. An example of a SB ETF is the Vanguard Dividend Appreciation Index Fund which tracks companies that historically exhibit the behavior of increasing dividends and are likely to continue this trend. While this SB ETF is fundamentally weighted, meaning that holding weights are determined by specific factors such as earnings, profits, or in this case dividends, SB ETFs can employ other weighting strategies such as factor-based or traditional market-cap based.

This strategy is thus a hybrid of active and passive investing as the only time companies are incorporated into or divested from the ETF is when they meet or diverge from the established ruleset. While there is scarce research into SB ETF performance, there is a growing academic dialogue. Some claim that sponsors have too much discretion in creating SB ETFs and that data mining is the culprit behind claims of increased alpha generation.[7] However, other research shows promising results for SB ETFs, at least when they are correctly positioned. Cesario Mateus and Irina Mateus, found that only 40% of SB ETFs outperformed their peer market cap weighted ETFs in their paper *Do Smart Beta ETFs Deliver Persistent Performance?* Although

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[6] Malkiel, Burton Gordon. *A Random Walk down Wall Street: The Time-Tested Strategy for Successful Investing*. W.W. Norton & Company, 2020.

[7] Huang, Shiyang, Yang Song, and Hong Xiang. "The smart beta mirage." *Journal of Financial and Quantitative Analysis* (2020): 1-32.

this initial conclusion seems disheartening for SB ETFs, there was a large disparity in performance based mainly on ETF investment strategy.[8] Across all size segments: small-, mid-, and large-cap, growth focused SB ETFs not only outperformed value-oriented SB ETFs, they also generated greater returns than their peer comps. Small-cap growth SB ETFs returned 64% positive alpha and the mid-caps returned 54% positive alpha. The best performing segment was large cap growth with 67% of observed SB ETFs returning positive alpha in excess of their peer comps. However, this result was drowned out by the abysmal performance of large cap value SB ETFs which brought back 89% negative alpha compared to its comparable traditional ETF. Value oriented SB ETFs in the small-, and mid-cap segments performed equally as poorly.

This makes sense fundamentally considering that large cap value ETFs generally focus on GDP-locked markets because they are traditionally safer. Overall market growth in these mature industries is primarily driven by inflation rather than innovation, market expansion, increased consumption, or any other typical growth driver. While active value investors can stock pick securities who are trading at a discount, due to the diversified nature of value focused ETFs the discounted companies are generally balanced out by the securities trading at a premium in the portfolio. Growth oriented ETFs, however, focus on companies and markets that are still in the introduction and growth phases of their market lifecycle. This means they can achieve growth greater than mere inflationary gains and thus more consistently create positive alpha. An ETF is also best suited to reap the overall market gains in this segment as growth markets are typically characterized by high competition and no clear industry leaders. Where there is equal opportunity for competitors to seize market control in the future, the best investment strategy is

[8] Mateus, Cesario, Irina B. Mateus, and Marco Soggiu. "Do smart beta ETFs deliver persistent performance?." *Journal of Asset Management* 21 (2020): 413-427.

to diversify holdings to minimize unsystematic risk as is done with an ETF. This is why the growth ETFs consistently and significantly outperformed the value oriented SB ETFs.

To summarize, there are three main ETF investment strategies, (1) passive, (2) active, and (3) SB ETFs. When looking at mature, value-oriented industries or companies, a passive approach is typically best. In this case, index investing can be used to generate some of the best risk-adjusted returns possible. However, growth-oriented SB ETFs have been shown to consistently create positive alpha in comparison to peer market-weighted ETFs. This means that SB ETFs, when correctly positioned in growth markets, are one of the best investment vehicles available to retail traders.

Transition to Custom ETFs

Historically, ETFs have been products created and managed by large financial institutions. However, there are a few troublesome items with this arrangement. First, the ETF is being managed by a third party and that means less control in the hands of the retail trader. While this is best for some investors with a completely hands-off approach, it is not for everyone. Second, ETFs generate returns on a post-expense basis. Similar to mutual funds, ETFs typically have "Annual Fund Operating Expenses" that reduce returns.[9] Lastly, while there are ETFs available for almost every market and industry, institutions can sometimes be slow to create ETFs for new and growing markets. Because they are institutional products, they take time and labor to be curated and listed to an exchange. This means crucial time out of the market in rapidly emerging sub-industries and sub-markets.

[9] "Mutual Fund vs ETF: What's the Difference?" *FINRA.Org*, 10 Nov. 2022, www.finra.org/investors/insights/etf-vs-mutual-fund?gad_source=1&gclid=Cj0KCQjw2PSvBhDjARIsAKc2cgOUgywMlMNUzILAncsr4XLTXcUEyO2cf3DzqtP4vKM07qa4qaEiGIQaAtCOEALw_wcB.

Considering these drawbacks, a new trend in the ETF space is for retail traders to create their own custom ETFs. These custom ETFs are similar to SB ETFs in that they are typically ruleset determined but they operate as mini portfolios within one's overall retail portfolio. By creating a mini portfolio in such a fashion, a retail trader can gain exposure to rapidly growing industries while minimizing concentration risk associated with individual securities.

Ralph Birchmeier, CPA, CFA, and former Principal at Brandes touches on this tactic in his 2023 book *Reasons to Pass*. Birchmeier highlights the advantages of indexing early on saying it is, to a large extent "good for clients, good for the system, and good for active investors" (63). In his defense of the transition to indexed funds from actively managed funds he states both structural reasons, namely lower fees, and cyclical elements: fee pressure, index funds proven returns, and increased asset flow into index fund driving returns for "in" index names. As previously discussed, these reasons for a transition to indexing are provocative and they have led to a large increase in available ETFs which follow a passive, index-based approach. However, Birchmeier also highlights that a "problem arises when a good idea, such as indexing a portion of one's assets, goes too far" (68). His main qualm with over-indexing one's assets is that indexes do not differentiate between the specific type of unsystematic risk present in "in" index names. Although you hedge one company's risk against the other indexed companies, when your index is market-cap weighted you may become overexposed to certain, riskier, mega-caps because there are no other investment criteria besides market cap.

Smart-Beta and custom ETFs attempt to minimize this risk by creating specific inclusion and weighting principles, but Birchmeier has other ideas as well. Primarily relevant to this work are his investment options: (6) out of index names, (7) small-cap stocks, and (10) baskets of similarly exposed names. This last option, baskets of similarly exposed names, is one of the key fundamentals behind custom ETF creation. As Birchmeier explains “individually speculative stocks have no place in a concentrated portfolio,” because “the risk of permanent impairment is too high” (273). However, in specific circumstances, there is a viable strategy to invest in speculative industries “through the construction of a basket of similarly exposed names in smaller individual allocations to diversify risk” (273). This is the foundational idea behind custom ETFs and why they can be utilized to gain exposure to high growth markets.

There are four main characteristics which make a market ideal for a custom ETF. A custom ETF is best for (1) fragmented or very diverse markets with (2) intense competition, (3) high market growth potential, and (4) no clear indicator of a future market leader. These characteristics generally constitute the speculative markets and securities Birchmeier discusses. In these markets a custom ETF is the best form of investment because it will be able to generate returns based on systemic market growth through diversified holdings. Though some holdings are bound to fail due to the intense competition, these costs are generally negated by the alpha created by market winners and total market growth.

I will now begin the second section of this study in which I will demonstrate how a retail trader can take advantages of the proven alpha-generating potential of growth-oriented SB ETFs by creating a custom ETF aimed at the rapidly growing oncology pharmaceuticals industry.

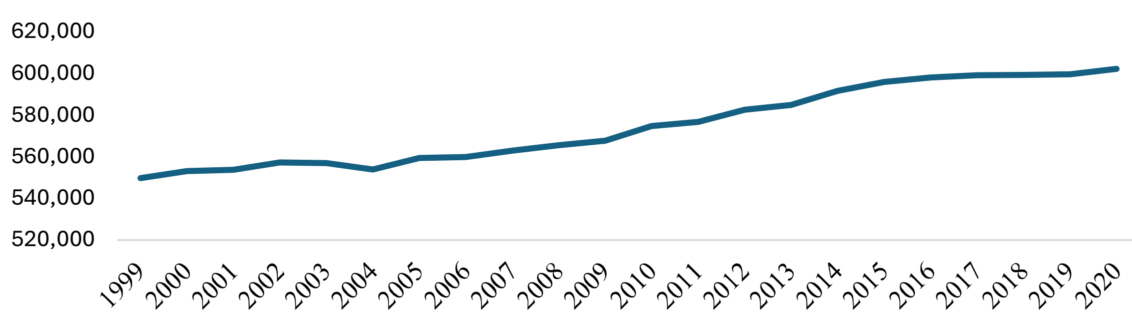
Part 2: Creating a Custom ETF

The Oncology Economy

The Cancer Epidemic

Cancer is now the second leading cause of death in the US, accounting for roughly 18% of all US deaths in 2021. With longer lifespans and increased exposure to carcinogens, both cancer diagnoses and deaths have been steadily growing for decades. From 1999 to 2020 cancer deaths in the US increased by 9.5%. Sunlight, tobacco, pharmaceuticals hormones, alcohol, parasites, fungi, wood dust, and much more can all cause cancer. Cancer is also not one specific ailment but rather an umbrella term for a "large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue."[10] There are over 100 known types of cancer. Some are very prevalent with better survival rates, such as breast or prostate cancer, while others are less common but have higher mortality rates, such as lung cancer. Among all these cancers, though, there is still no surefire cure. There are new and innovative treatments, novel pharmaceuticals, cutting edge therapies, but no consistent way to prevent or cure cancer.

Figure 2: Total Cancer Deaths in the US 1999-2020[11]



[10] https://www.mayoclinic.org/diseases-conditions/cancer/symptoms-causes/syc-20370588#:~:text=Cancer%20refers%20to%20any%20one,of%20death%20in%20the%20world.
[11] CDC. "Total Number of Cancer Deaths in The United States from 1999 to 2020." *Statista*, Statista Inc., 25 Oct 2023, https://www.statista.com/statistics/533808/number-of-cancer-deaths-in-us/

Figure 3: 2022 World Cancer Deaths by Type (%)

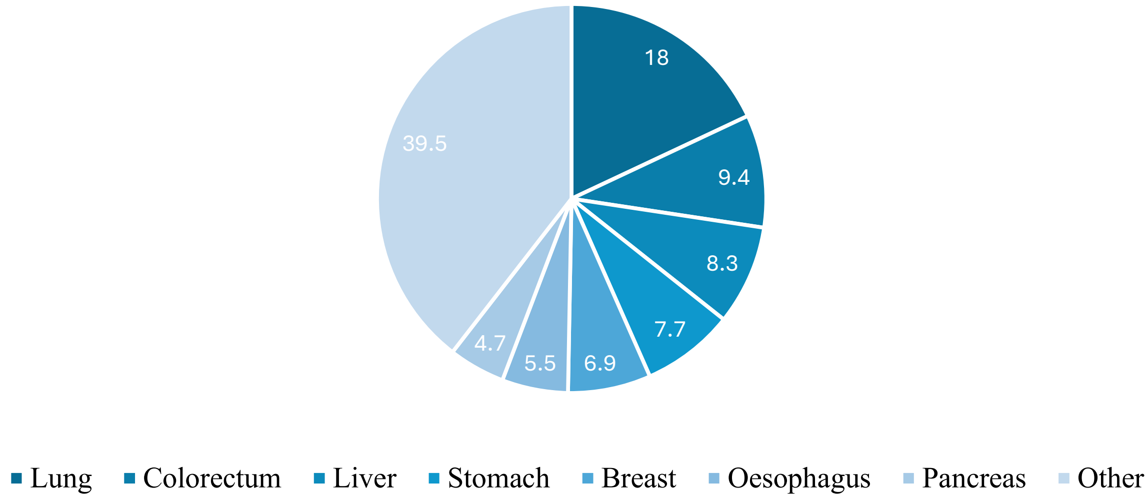


Figure 3: Above shows 2022's total world deaths by cancer type. While death rates differ from diagnosis rates, there are apparent weaknesses in Lung oncological research specifically. This is due primarily to the late diagnosis of lung cancer as symptoms manifest late. Additionally, metastasis is highly likely from lung cancer as there is significant blood flow through the area. While some types of deadly cancer, such as breast and prostate cancer, have had significant innovation, other areas lag behind and are prime for new detection and treatment methods. [12]

Figure 4: Estimated Number of New Cancer Cases 2020-2040

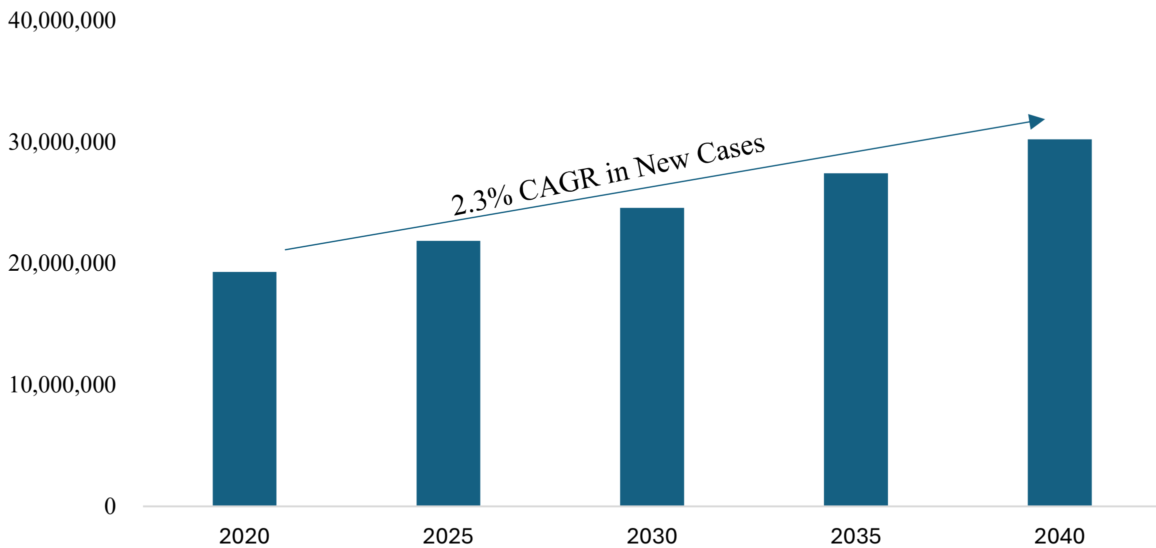


Figure 4: There is a 2.3% predicted increase in new cancer cases per year through 2040. With increasing death rates as well due to the prevalence of more deadly cancer types such as lung and stomach cancer, this will mean significantly more spending in the oncology economy. Though all efforts are being taken to understand and treat these hard to detect, and high risk to treat diseases, there will still be significant suffering caused by the cancer epidemic in years to come. [13]

[12] WHO, and International Agency for Research on Cancer. "Number of Cancer Deaths Worldwide in 2022, by Major Type of Cancer." *Statista*, Statista Inc., 26 Apr 2024, https://www.statista.com/statistics/288580/number-of-cancer-deaths-worldwide-by-type/

[13] WHO, and International Agency for Research on Cancer. "Predicted Number of New Cancer Cases Worldwide from 2022 to 2050." *Statista*, Statista Inc., 29 Apr 2024, https://www.statista.com/statistics/1031316/new-cancer-cases-forecast-worldwide/

The Oncology Economy

As cancer has grown more prevalent, it has built a large economy around it. Businesses now work to prevent, detect, treat, monitor, and research all types of cancer with varying success. The global oncology market was estimated to be $218 billion as of 2023 and it is projected to have an annual growth rate of 16% through 2027. This makes the cancer economy one of the quickest growing segments of the healthcare industry.

Figure 5: 2022 Oncology Market Share by Company

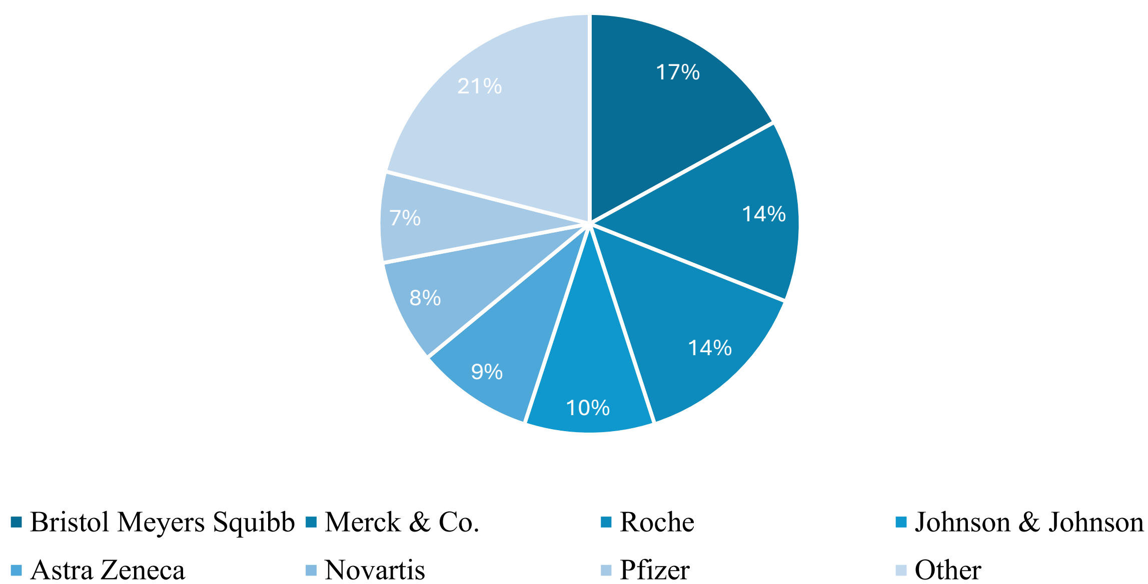


Figure 5: This pie chart breaks down total market share of the oncology pharmaceuticals market according to research conducted and conglomerated by Statista. BMY is number one, closely followed by AZN and MRK. All others account for less than 10% of the market each. [14]

This rapidly growing market is split between hospitals and pharmaceutical companies. Hospitals have captured roughly 60% of the market with diagnostics, treatments, therapies, room charges, and other related services. The other 40% is occupied by big pharma companies such as Bristol Meyers Squibb (BMY) and Merck & Co. (MRK). Despite the skewing in market share

[14] Statista Market Insights. "Oncology Drugs - Worldwide: Statista Market Forecast." *Statista*, www.statista.com/outlook/hmo/pharmaceuticals/oncology-drugs/worldwide?currency=usd#key-players. Accessed 30 Apr. 2024.

towards hospitals, due to the large amount of non-profits and specialized hospitals without potential for investment, pharmaceuticals are the main choice for putting capital to work in the oncology economy. Considering the estimated CAGR of 16%, by 2027 these big pharma companies will have access to a $150 billion market for oncological drugs.

To capture this substantial and rapidly growing market, pharmaceutical companies are currently in intense competition. In-house R&D is at an all-time high and the oncology acquisition market is hot as strategics engage in bidding wars for the most reputable and promising oncology startups and SMEs. Currently, cancer accounts for 12 of the top 15 diseases with the most active drugs worldwide. That means that oncology-focused pharmaceutical companies are researching, producing, and maintaining more drugs for cancer than any other disease. This is a reaction not only to the large market potential, but to the fact that there is no clear market leader. Competition is currently driving innovation at a breakneck pace in the oncological drugs market as a key breakthrough to curing cancer could be the key to establishing prolonged market dominance.

These facts make the oncology pharmaceuticals market a great candidate for a custom ETF. While there is market consolidation among the top strategics, there is no clear market leader and innovation is the current key to success. The high market competition increases consolidation risk as any one company could experience a downturn or lose market share; however, the consolidation risk is outweighed by the high market growth potential. A diversified, growth ETF could thus take advantage of overall market gains while minimizing unsystematic risk associated with stock picking in such a volatile environment. Considering these elements, the oncology pharmaceuticals market thus meets requirements (1) through (4) as previously detailed and is a prime candidate for a custom growth ETF.

Below, I will lay out my process for creating said ETF as well as the final holdings and weightings of the experimental ETF.

The Oncology ETF - The (ONC) ETF

Current Oncology ETFs

In recent years there has been a rise in the number of oncology-focused ETFs available in the market. The most relevant to my study are Tema's Oncology ETF (CANC) and Range's Cancer Therapeutics ETF (CNCR). While the creation of new ETFs focusing on the oncology space is promising, both CANC and CNCR have some issues. CANC is a mid-cap growth-oriented SB ETF with a very experienced management team. Its inclusion principle of companies generating 50% of revenues from cancer services excludes companies which are moving into the oncology space more heavily, such as JNJ, from being included. Additionally, it is still experimental as it was released in August of 2023, meaning there is little data to review actual performance. CNCR is the original cancer-oriented ETF. It is a small-cap blended approach ETF founded in 2015. However, since its release onto the NASDAQ, it has returned (42.98)% to date. While CNCR was overhauled in 2023 to become Range Cancer Therapeutics ETF, from previously being the Loncar Cancer Immunotherapy ETF, it is yet to be seen how the ETF will perform moving forward. Both ETFs also have management fees similar to all other ETFs. Though they are both low, only 0.75% and 0.79% respectively, and necessary for the curation and maintenance of the ETFs, these fees do still detract from investor gains.

ETF Selection Criteria

I began my selection process by setting an initial list of inclusion principles. Throughout my research this initial list was refined into the following:

1. Large market cap companies – above $10B
2. 20% or more of revenue reinvested in research and development (R&D)
3. Strong and consistent M&A
4. Strong focus on oncology with minimal distractions from other operational segments

With these criteria, I am attempting to compensate for what I view to be the shortcomings of CANC and CNCR that have led them to lackluster returns. Both CANC and CNCR attempt to mitigate the risk profile of smaller cap companies with holdings in more stable larger companies; however, considering the operational, financing, and risk differences between large, mid, and small cap companies I believe it best to create an ETF with only large cap companies. This way the basket is truly of similar companies. Additionally, if I desire exposure to smaller companies in the future, I can create another miniature portfolio of small caps which has a different operational, financing, and risk profile from the large cap portfolio.

Additionally, both ETFs have some underlying requirement of amount of revenue stemming from oncology, but this does not ensure the company is properly progressing in the space. For this reason, I took out the quantitative revenue requirement and replaced it with a quantitative R&D requirement in addition to a more general M&A requirement.

The R&D requirement seeks to ensure the company is confident enough in its internal capabilities to invest heavily in future offerings. It is also insurance that the company is indeed putting out new drugs as patents come due. The M&A requirement ensures the company is covering its bases and recognizes opportunities in the market which it cannot replicate in-house. As previously mentioned, the pharmaceutical space in general is largely driven by M&A activity. Startups and SMEs are the innovators and disruptors of the space. As they produce new drugs and technologies, these large strategics I am analyzing should look to acquire promising companies to expand their offerings past what is capable with mere R&D.

Lastly, I put in the general consideration that portfolio companies should have limited additional operational segments outside of pharmaceuticals. Companies with MedTech and Consumer Health segments in addition to Pharmaceuticals are too spread out to take full advantage of the future growth in the oncology economy. Considering the intense competition, portfolio companies should have their main focus be pharmaceuticals with an emphasis on oncology.

<u>Big Pharma M&A Discussion & Exhibits:</u>

<u>Figure 6: Total Pharma M&A Spend by Year ($M)</u>

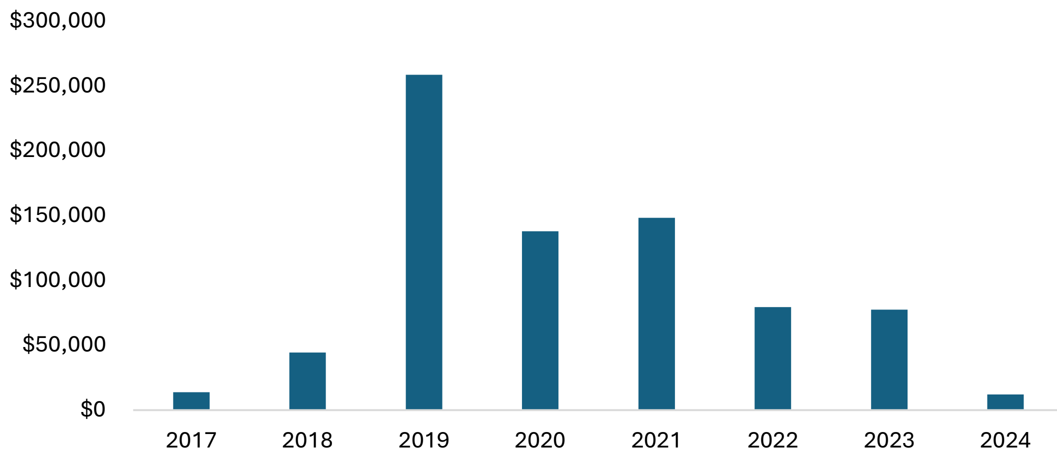


Figure 6: This bar chart depicts total buyside M&A activity of all pharmaceuticals companies from 2017 to 2024. During the pandemic, ZIRP era, M&A activity was very active and many companies engaged in mergers, acquisitions, and strategic investments to expand their offerings and consolidate the market. However, with the Inflation Reduction Act (IRA) threatening to cut earning potential on top selling drugs, many pharmaceuticals companies have began building up their cash reserves and slowing down engaging in costly operating and growth activities such as M&A.

Figure 7: The "Big 7" Pharmaceutical M&A Spend by Year ($M)

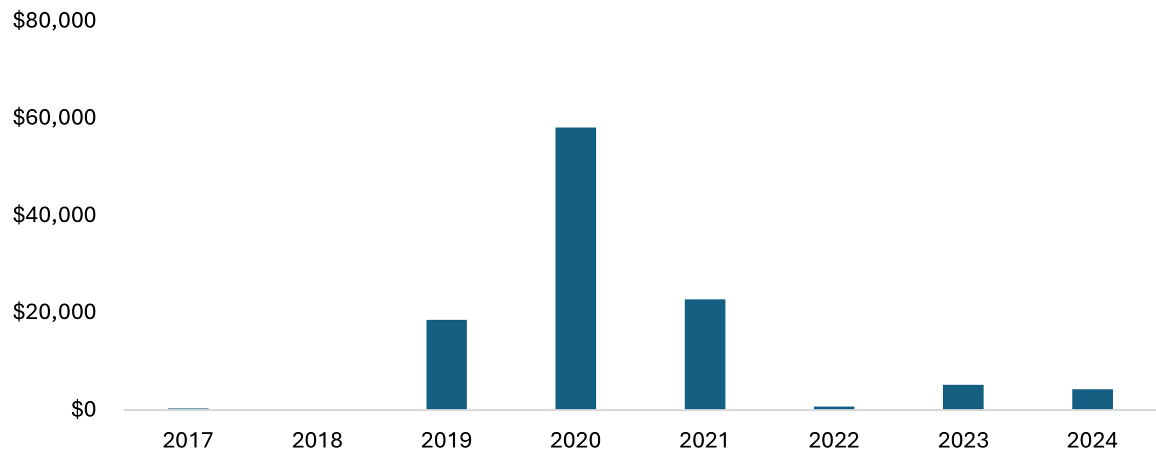
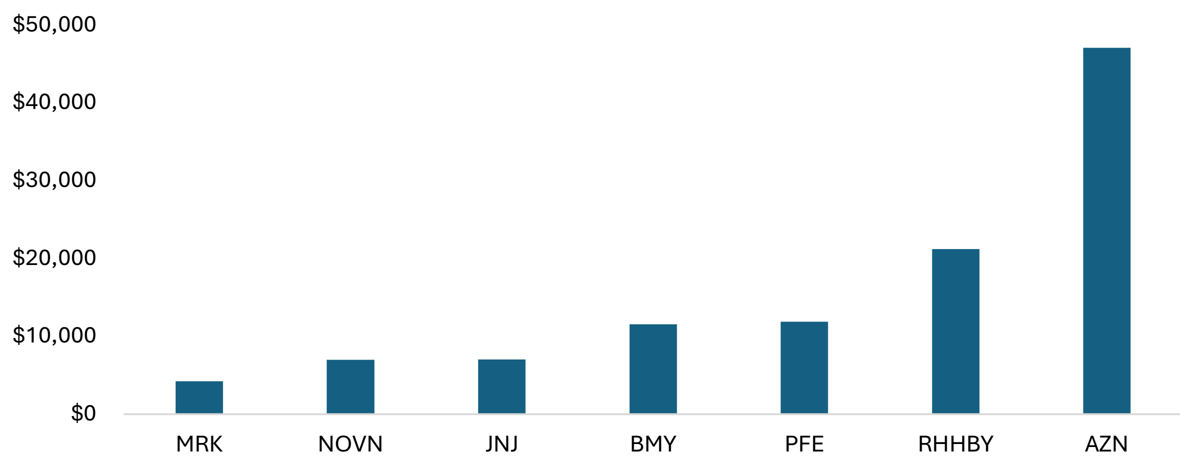


Figure 7: Above shows total M&A activity from the "Big 7" in the same time frame as the previous figure. In similar fashion, the Big 7 engaged in massive M&A activity during the pandemic while multiples were compressed and debt was cheap. In 2020 they were roughly 1/3 of all pharmaceutical buyside activity. Although current spend is lower than pandemic historical data, they are beginning to fall into a comfortable medium of dedicating cash flow to M&A, thereby hedging potential risk from the IRA while continuing to consolidate the market and expand offerings.

Figure 8: The "Big 7" Pharma M&A Spend ($M)



Graph 8: The bar chart above shows total Big 7 M&A spend over the same 5-year period as Figure 7, however, it is segmented by company. The largest player was Astra Zeneca (AZN) due to their $43.3B acquisition of Alexion Pharmaceuticals in 2021. Alexion researched, developed, and distributed therapeutic drugs for rare diseases and cancer. Since their acquisition, AZN stock has risen nearly 40%. [15]

The graphs above show the importance of M&A in the pharmaceuticals industry to drive growth, competition, innovation, and most importantly shareholder returns. As seen with Astra Zeneca's successful acquisition of Alexion Pharmaceuticals in 2021, M&A can be a potent and effective method to drive shareholder returns and gain market share through expanded and

[15] Bloomberg Market Research

improved offerings. M&A activity allows pharmaceuticals companies to essentially create their own portfolios of offerings, acquiring companies that fit their specific need or meet certain blind spots and then potentially divesting them down the line if the specific offerings stagnate or decrease or the company changes focus or strategy. For these reasons I made M&A in addition to a quantitative R&D requirement necessary for inclusion in the ETF.

<u>ETF Selection Process</u>

With my preliminary selection criteria in place, I started to parse through the existing oncology ETFs, (CANC) & (CNCR), to identify any overlapping large market cap companies. The more modern CANC is made up of 32% large cap, 19% medium cap, and 28% small cap companies. It also only has 47 equities in comparison to CANC's 78 total equities. CANC is made up 6% large cap, 26% medium cap, and 68% small cap companies. Both ETFs also have money market investments to hold cash for future entries.

In total, there were 23 overlapping companies. Of these 4 were large cap companies. Put differently, 4 of the 5 large caps that CANC invested in, CNCR also invested in, which means they were a strong starting place for analysis. These four securities were MRK, REGN, BMY, and GMAB. Ultimately, all except GMAB were included in the ETF. I decided to remit GMAB due to its lackluster M&A. Despite phenomenal historical growth and nearly 50% of revenues being recycled into R&D, they have only made a few acquisitions and thus could easily be outpaced by larger strategics investing more heavily in promising targets.

Next, I looked at the "Big 7," or the 7 largest players in the oncological pharmaceuticals space. This list consisted of BMY, MRK, RHHBY, JNJ, AZN, NOVN, and PFE. Unsurprisingly, there was some overlap with the previously selected large caps from my existing ETF analysis.

These companies also represent the largest M&A spenders in space, per Bloomberg research. However, their M&A expenditures, as with most other companies, is largely cyclical and is currently being threatened by a potential decrease in revenues from the Inflation Reduction Act (IRA). The Biden administration initially announced cost regulation on 43 prescription drugs; however, that number has changed due to some lobbying and negotiations from big pharma. Ultimately, however, these companies being both market leaders and the most active strategics meant they were excellent for further analysis.

All companies except JNJ and PFE were included in the ETF from the “Big 7.” Both JNJ and PFE had lackluster R&D, which was historically below 20% of revenues, and had other large operational segments which could potentially distract from oncological research. I have included a one pager of JNJ after the ETF proposal as an example of my analysis leading to pass decisions.

Finally, I parsed through the last of the large cap companies in both oncology ETFs and completed several screens on Bloomberg to look for promising companies. These efforts resulted in the inclusion of Gilead Sciences, Inc. (GILD), Illumina, Inc. (ILMN), and Incyte Corp. (INCY). There were many other promising candidates, such as Exact Sciences (EXAS) which exclusively focuses on cancer screening; however, these companies would typically fail my R&D or M&A inclusion principles.

<u>Portfolio Weighting</u>

I determined ideal portfolio weightings via optimizing total portfolio Sharpe ratio considering expected annualized 5-year returns. 5-year returns were determined as an average of my intrinsic valuations on base cases. Ideal portfolio size was then determined by approximating actual weightings as closely possible to ideal weightings. The limiting factor here was REGN, as it was one of the lowest weighted holdings at 5% yet was the most expensive at $900. This meant that total portfolio allocations needed to be close to $18,000, and using Excel solver I found that total allocations would be ideal at $17,902. Although this is rather large for an average retail portfolio, by excluding REGN the total allocation can be brought down to roughly $4,000 while maintaining allocation integrity.

Figure 9: ETF Weighting Process

Ticker	Avg Exp	Current Price	Expected Price	Expected 5 Yr CAGR	Historical STDEV	Min Weight	Max Weight	Optimal Weighting
MRK	30%	$ 126.94	$ 165.02	5%	0.015	5%	20%	5%
AZN	42%	$ 70.13	$ 99.34	7%	0.017	5%	20%	5%
RHHBY	81%	$ 30.91	$ 55.92	13%	0.015	5%	20%	20%
NOVN	63%	$ 95.12	$ 154.57	10%	0.013	5%	20%	15%
BMY	109%	$ 40.14	$ 83.73	16%	0.014	5%	20%	20%
REGN	16%	$ 900.16	$ 1,040.13	3%	0.020	5%	20%	5%
GILD	104%	$ 66.95	$ 136.24	15%	0.016	5%	20%	20%
ILMN	40%	$ 120.25	$ 168.47	7%	0.028	5%	20%	5%
INCY	51%	$ 51.92	$ 78.53	9%	0.020	5%	20%	5%

Portfolio Statistics	
Sharpe Ratio	4.14
Expected Annual Return	11.8%
STDEV	0.02
Total Weight	100%

Assumptions	
RFR	5.25%

Actual Portfolio Statistics	
Sharpe Ratio	4.17
Expected Annual Return	11.9%
STDEV	0.02
Portfolio Beta	0.34
Total Weight	100%

Ticker	Optimal Weighting	Optimal Allocation	Actual Units	Actual Allocation	Actual Weighting
MRK	5%	$900	7	$889	5.0%
AZN	5%	$900	13	$912	5.1%
RHHBY	20%	$3,600	116	$3,586	20.0%
NOVN	15%	$2,700	28	$2,663	14.9%
BMY	20%	$3,600	90	$3,613	20.2%
REGN	5%	$900	1	$900	5.0%
GILD	20%	$3,600	54	$3,615	20.2%
ILMN	5%	$900	7	$842	4.7%
INCY	5%	$900	17	$883	4.9%

ETF Goal Size	$18,000
Actual ETF Size	$17,902

Figure 9: The above excel clipping depicts the ETF's weighting process. Step one involved determining historical standard deviation of returns in addition to expected yearly returns for my 5 year projection period. Using these as well as an assumption of 5.25% for the risk free rate, I found that optimal portfolio allocations resulted in a Sharpe ratio of 4.17. This is driven by the large growth potential, estimated to be roughly in line with general market returns, with a significantly lower risk profile. Total portfolio beta came out to roughly one third of the general market, 0.34, and portfolio STDEV of returns was more consistent than SPY. While some of the smaller companies such as ILMN and INCY had higher risk profiles, they were ultimately weighted at the minimum.

Disclosures Regarding Sources Used to Research and Create the Oncology ETF

Most of my research could be conducted using publicly available information via the SEC's EDGAR, Yahoo Finance, and other free and subscription-based sites. However, to streamline the analysis process, I used resources available to me through LMU's vast database subscriptions. I sourced all financial information from Capital IQ; however, I did have to check certain adjustments made by their analysts with SEC filings to verify their appropriateness for use in my analysis. All historical M&A information as well as WACC estimates were sourced from Bloomberg. Diluted shares outstanding was calculated using the most recent 10-K or 10-Q filings and considered all outstanding options, RSUs, PSUs, and any other stock compensation plans. All general stock information including market cap, 52-week range, 5 year beta, and historical stock data was sourced from Yahoo Finance. General valuation model formatting was sourced from LMU's Valuations class; however, some aspects were sourced from Wall Street Prep's available model templates. Finally, I conducted most of my analysis and am writing this thesis on Office subscriptions which are generously provided by LMU. Finally, all literature review in the first section of this work was made possible by LMU's large library, database subscriptions, and academic paper offerings. With these disclosures out of the way, let us dive into the ONC ETF.

Oncological Pharmaceuticals Index

Unit Cost:	1 Year Return:	5 Yr Annualized:	Beta:	Industry	As of:
$17,902	(18.8%)	2.1%	0.34	Healthcare	April 17, 2024

Index Overview:

Ticker	Optimal Weighting	Optimal Allocation	Actual Units	Actual Allocation	Actual Weighting
MRK	5%	$900	7	$889	5.0%
AZN	5%	$900	13	$912	5.1%
RHHBY	20%	$3,600	116	$3,586	20.0%
NOVN	15%	$2,700	28	$2,663	14.9%
BMY	20%	$3,600	90	$3,613	20.2%
REGN	5%	$900	1	$900	5.0%
GILD	20%	$3,600	54	$3,615	20.2%
ILMN	5%	$900	7	$842	4.7%
INCY	5%	$900	17	$883	4.9%

Goal Portfolio Statistics	
Sharpe Ratio	4.14
Expected Annual Return	11.8%
STDEV	0.02
Total Weight	100%

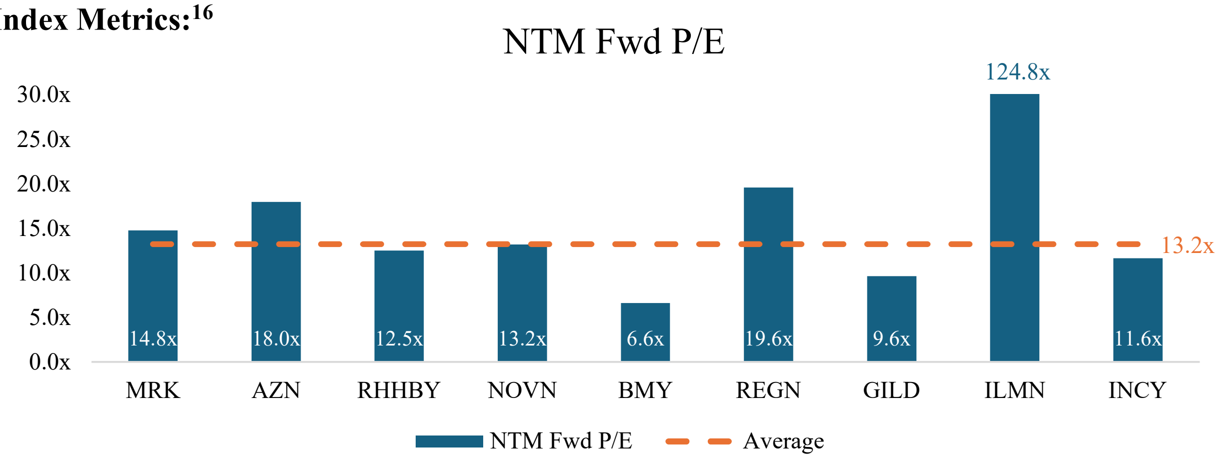
Actual Portfolio Statistics	
Expected Sharpe Ratio	4.17
Expected Annual Return	11.9%
Historical STDEV	0.02
Portfolio Beta	0.34
Total Weight	100.0%

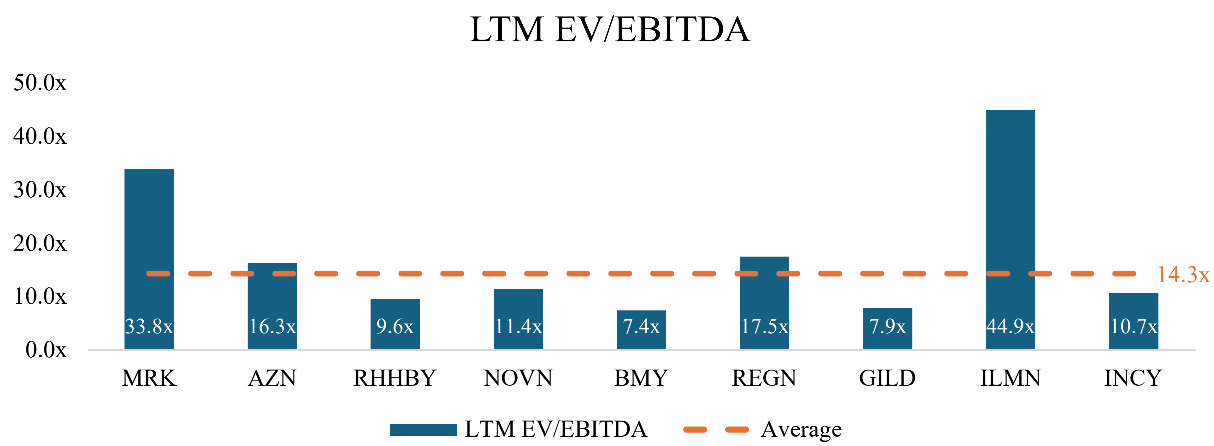
Assumptions	
RFR	5.25%

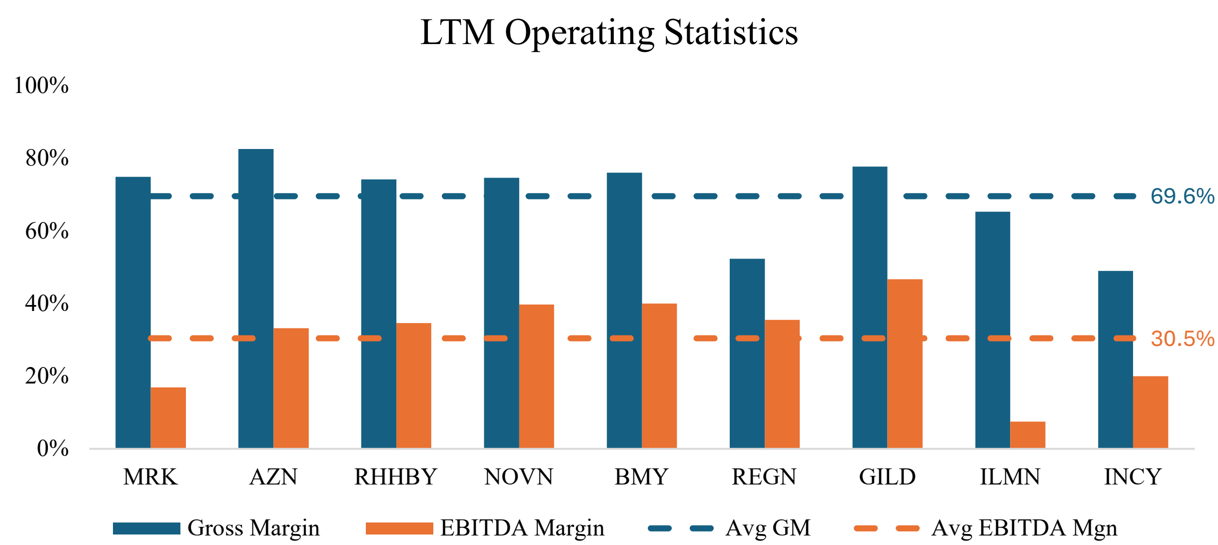
Inclusion Principles:

1. Large market cap companies – above $10B
2. 20% or more of revenue reinvested in company via R&D
3. Strong and consistent M&A – either Big 7 or clear M&A trends
4. Strong Oncological offerings/pipeline
5. Limit of 1 non-pharma operational segment to limit operational distractions

Index Metrics:[16]







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[16] *note* NTM Forward P/E and LTM EV/EBITDA averages exclude ILMN as a portfolio outlier. While ILMN's NTM Fwd P/E will be an improvement from their historically negative P/E, I do not believe it to be representative of the other stocks and drastically increases average P/E. The same applies for its EV/EBITDA, which will likely decrease to a peer comparable as operations improve and its EBITDA margin increases.

Merck & Co, Inc.

ETF Weight	Price	1 Year Return	NYSE:	Industry	As of:
5.0%	$125.28	8.29%	MRK	Healthcare	April 17, 2024

Business Description

Merck & Co., Inc. operates as a healthcare company worldwide. It operates through two segments: Pharmaceutical and Animal Health. The Pharmaceutical segment offers human health pharmaceutical products in the areas of oncology, hospital acute care, immunology, neuroscience, virology, cardiovascular, and diabetes, as well as vaccine products consisting of preventive pediatric, adolescent, and adult vaccines. The Animal Health segment discovers, develops, manufactures, and markets veterinary pharmaceuticals, vaccines, and health management solutions and services, as well as digitally connected identification, traceability, and monitoring products. The company serves drug wholesalers and retailers, hospitals, and government agencies; managed health care providers, such as health maintenance organizations, pharmacy benefit managers, and other institutions; and physicians, wholesalers, government entities, veterinarians, distributors, animal producers, farmers, and pet owners. It has development and commercialization agreement for three of Daiichi Sankyo's deruxtecan ADC candidates for the treatment of multiple solid tumors both as monotherapy and/or in combination with other treatments; and AstraZeneca PLC to co-development and co-commercialize AstraZeneca's Lynparza products for multiple cancer types, and Koselugo. Merck & Co., Inc. was founded in 1891 and is headquartered in Rahway, New Jersey.

MRK Overview

Market Cap:	317.566B
5 Yr Beta:	0.40
Dividend Yield:	2.46%

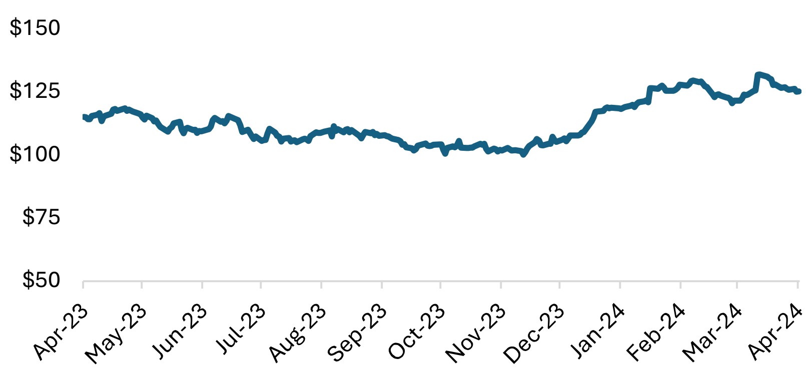
Operating Metrics

YoY Rev Growth:	1.0%
Gross Margins:	73.5%
Profit Margins:	*0.6%

***Multiples**

NTM P/E:	14.84x
EV/Sales:	5.85x
NTM EV/EBITDA:	12.05x

MRK LTM Stock Performance



MRK has experienced some appreciation following their 2023 acquisition of Promethius. Since then, they have been range bound as investors wait to see if they meet earnings expectations via the integration of Prometheus and continued success of Keytruda.

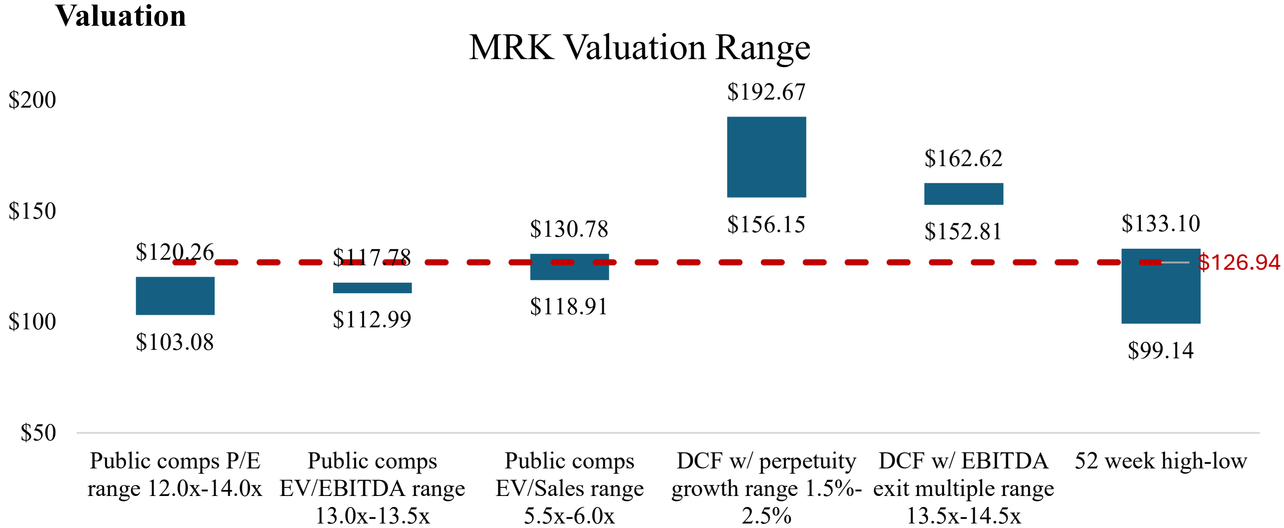
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	14,487	15,035	15,962	14,630
2022	15,901	14,593	14,959	13,830
2021	10,627	11,402	13,154	13,521
2020	10,288	9,353	10,929	10,948

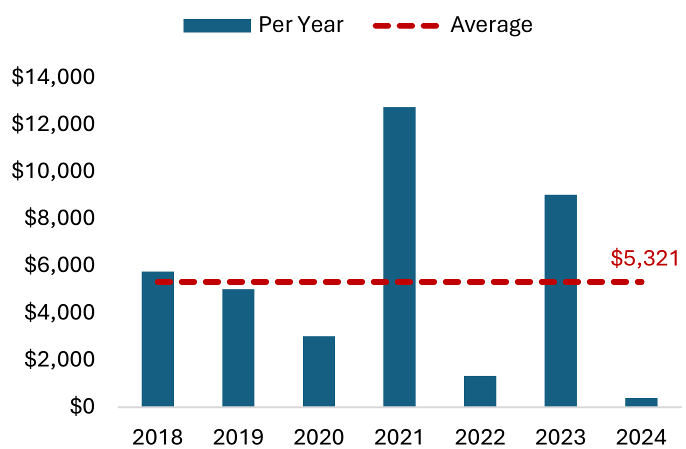
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	1.11	(2.35)	1.87	(0.48)
2022	1.70	1.56	1.28	1.19
2021	1.26	0.61	1.81	1.49
2020	1.21	1.19	1.16	(0.83)

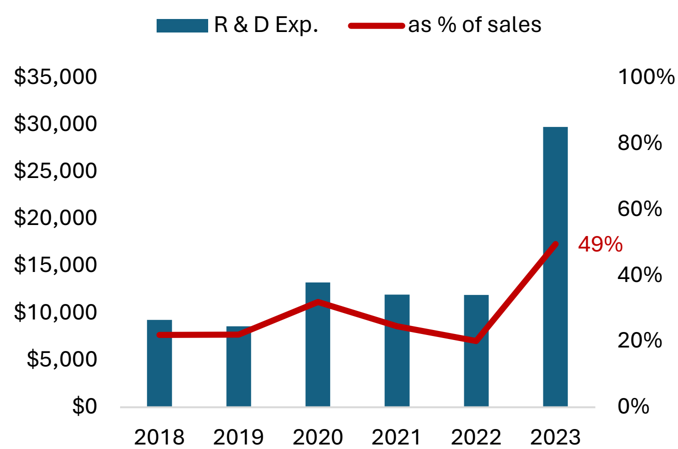
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

Merck currently produces, distributes, and owns the rights to the largest cancer drug in the world, Keytruda. Although their patent on Keytruda is set to expire in 2028, immense R&D as well as M&A efforts have several new drugs in clinical trials. They are currently focusing on DNA damage biology and cell-based therapies, two of the most up and coming segments in oncology. Recently, Merck bough Promethius for $10B. Prometheus has promising oncological offerings in addition to other treatments currently in clinical trials. While Merck is one of the more expensive companies of the portfolio, as seen by its LTM P/E of ~66x, it is nonetheless primed for further expansion and market domination.

Astra Zeneca PLC

ETF Weight	Price	1 Year Return	NASDAQ:	Industry	As of:
5.1%	$66.95	(7.46%)	AZN	Healthcare	April 22, 2024

Business Description

AstraZeneca PLC, a biopharmaceutical company, focuses on the discovery, development, manufacture, and commercialization of prescription medicines. The company's marketed products include Tagrisso, Imfinzi, Lynparza, Calquence, Enhertu, Orpathys, Truqap, Zoladex, Faslodex, Farxiga, Brilinta, Lokelma, Roxadustat, Andexxa, Crestor, Seloken, Onglyza, Bydureon, Fasenra, Breztri, Symbicort, Saphnelo, Tezspire, Pulmicort, Bevespi, and Daliresp for cardiovascular, renal, metabolism, and oncology. Its marketed products also comprise Vaxzevria, Beyfortus, Synagis, FluMist, Soliris, Ultomiris, Strensiq, Koselugo, and Kanuma for covid-19 and rare disease. The company serves primary care and specialty care physicians through distributors and local representative offices in the United Kingdom, rest of Europe, the Americas, Asia, Africa, and Australasia. It has a collaboration agreement with Neurimmune AG to develop and commercialize NI006. The company was formerly known as Zeneca Group PLC and changed its name to AstraZeneca PLC in April 1999. AstraZeneca PLC was incorporated in 1992 and is headquartered in Cambridge, the United Kingdom.

AZN Overview

Market Cap:	213.869B
5 Yr Beta:	0.19
Dividend Yield:	2.11%

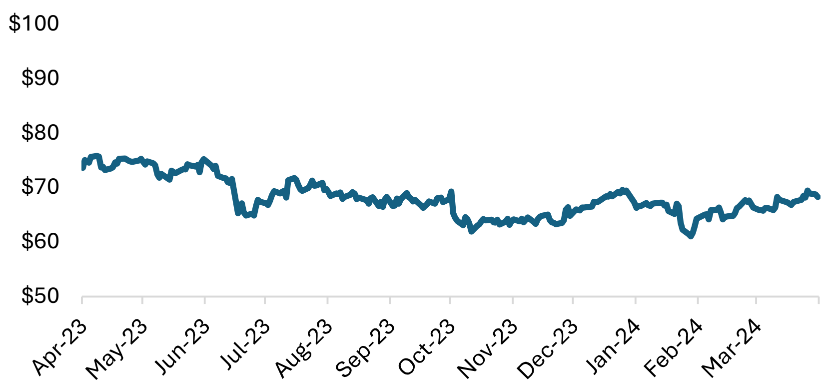
Operating Metrics

YoY Rev Growth:	(2.9%)
Gross Margins:	76.6%
Profit Margins:	17.9%

Multiples

P/E:	5.16x
EV/Sales:	15.49x
EV/EBITDA:	16.68x

AZN LTM Stock Performance



AZN has been largely range bound this past year as it has looked for potential M&A targets and continued with strenuous R&D activity. Though revenues have stagnated, EPS are increasing and it is to be seen if

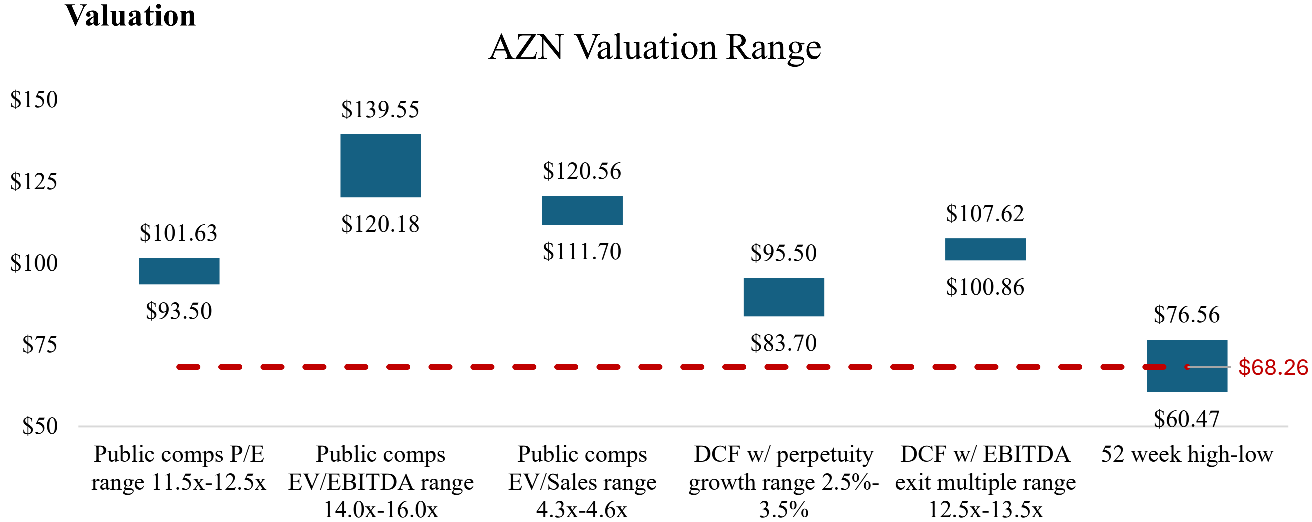
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	10,879	11,416	11,492	12,024
2022	11,390	10,771	10,982	11,207
2021	7,320	8,220	9,866	12,011
2020	6,354	6,275	6,578	7,410

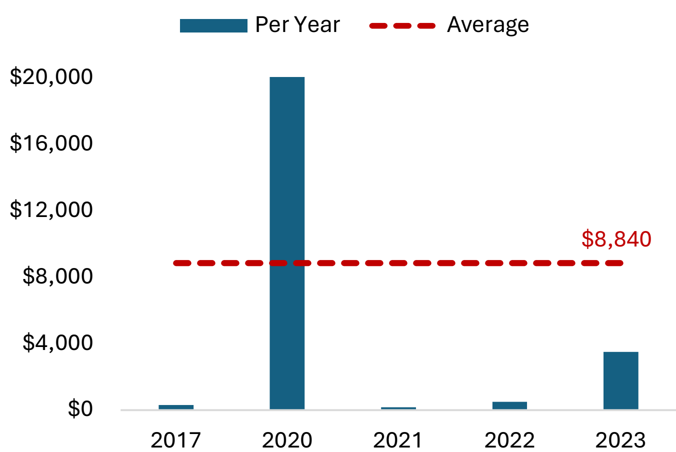
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	1.16	1.17	0.89	0.62
2022	0.25	0.23	1.06	0.58
2021	1.19	0.42		
2020	0.59	0.58	0.49	0.77

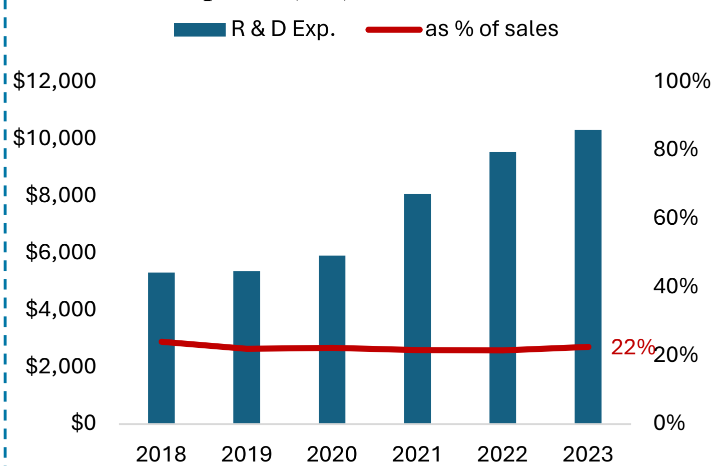
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

Though Astra Zeneca has experienced some sales stagnation in recent years, it has continually increased its EPS and has a strong pipeline of oncological offerings in stage 2 and 3 clinical trials. Since its $43B acquisition of Alexion Pharmaceuticals in 2021, AZN experienced initial appreciation and then eventual stagnation.

Investors currently seem to be gravitating towards other industry players with hotter offerings, however, AZN maintains the 5th highest grossing oncological treatment, Tagrisso. It also made some recent acquisitions to expand offerings. In 2023 AZN purchased CinCor Pharma for $1.8B, Gracell Biotechnologies for $1.2B, and Icosavax for $1.1B. These acquisitions are still being integrated into AZNs core operations, but they will cover some of the previous blindspots in AZN's offerings such as with cardiorenal diseases.

AZN's comparatively cheap P/E also makes it a great discount buy currently. With a wide international presence, diverse offerings, strong M&A and R&D pipeline for future offerings, and continual margin and EPS improvement, AZN meets all the criteria for inclusion.

Roche (ROG.SW)

ETF Weight	ADR Price	ADR 1 Yr	OTCM:	Industry	As of:
20.0%	$30.08	(22.23%)	RHHBY	Healthcare	April 17, 2024

Business Description

Roche Holding AG engages in the pharmaceuticals and diagnostics businesses in Europe, North America, Latin America, Asia, Africa, Australia, and Oceania. The company offers pharmaceutical products in the therapeutic areas of anemia, blood and solid tumors, dermatology, hemophilia, inflammatory and autoimmune, neurological disorders, ophthalmology, respiratory disorders, and transplantation. It is also developing products for various therapeutic areas. In addition, it offers in vitro tests for the diagnosis of various diseases, such as cancer, diabetes, Covid-19, hepatitis, human papillomavirus, and other diseases; diagnostic instruments; and digital health solutions. Roche Holding AG was founded in 1896 and is based in Basel, Switzerland.

RHHBY Overview

Market Cap:	195.544B
5 Yr Beta:	0.15
Dividend Yield:	4.63%

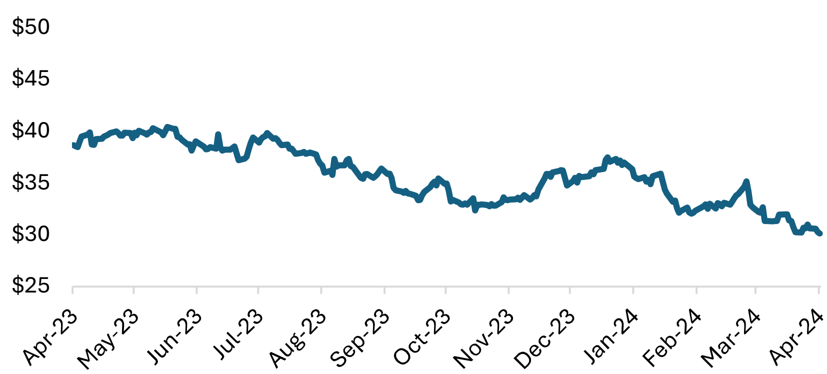
Operating Metrics

YoY Rev Growth:	(8.2%)
Gross Margins:	74.2%
Profit Margins:	19.0%

Multiples

P/E:	15.62x
EV/Sales:	3.38x
EV/EBITDA:	9.62x

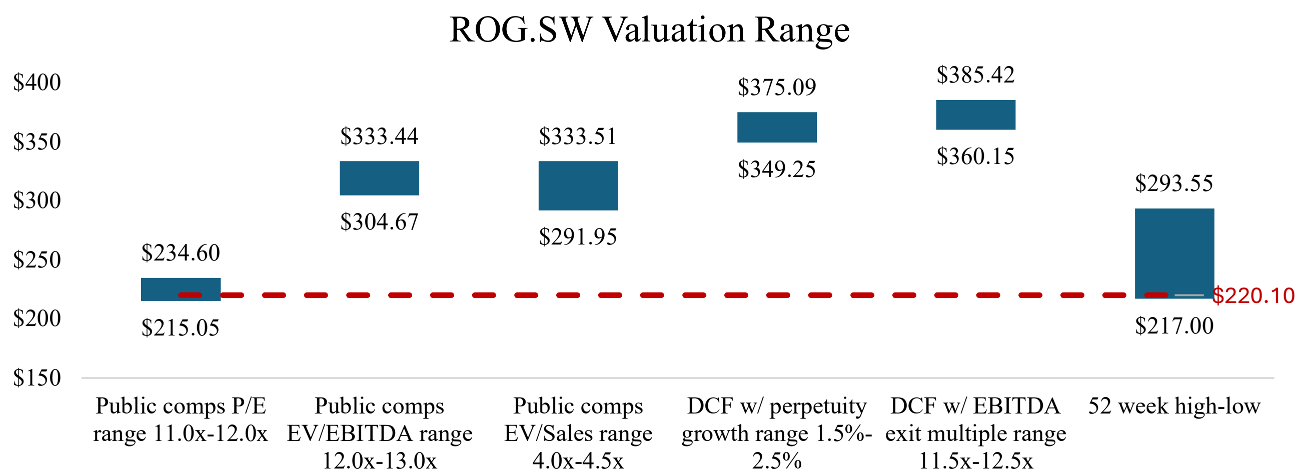
RHHBY LTM Stock Performance



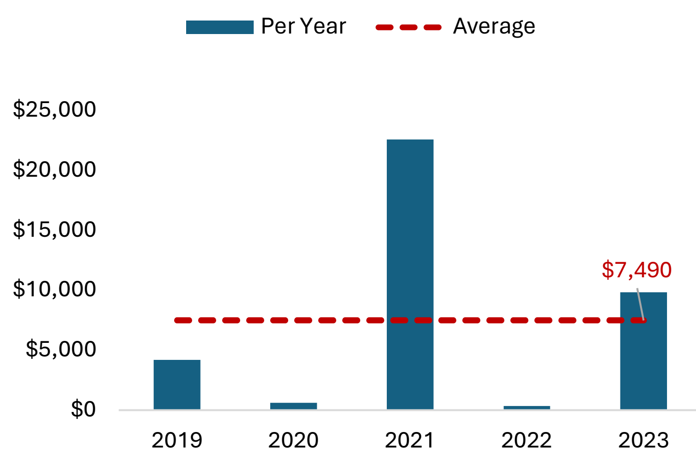
Roche experienced a downturn in 2023 with some important drug offerings experiencing stagnation and investor sentiment remaining undecided. With strategic acquisitions completed and a strong outlook for 2024 we wait to see if they rebound from this slump.

	Revenue ($M)				Earnings Per Share			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
2023	16,773	17,106	16,306	17,709	4.89	4.99	2.98	3.24
2022	18,406	17,750	16,258	17,257	5.78	5.58	2.48	2.63
2021	17,047	17,377	18,067	18,493	4.85	4.94	3.88	3.97
2020	15,763	16,038	16,333	16,934	4.90	4.99	3.96	4.11

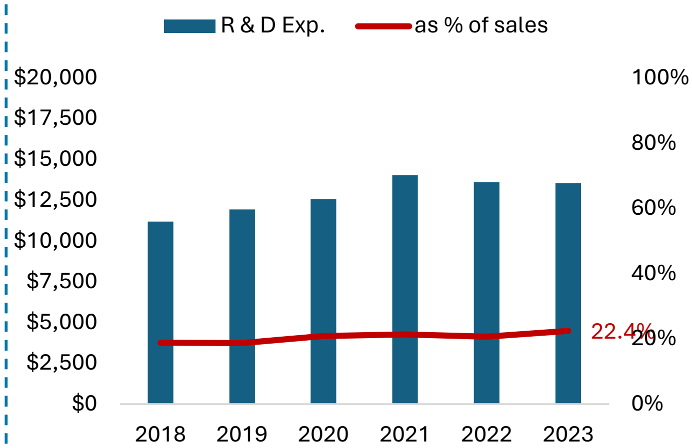
Valuation – ROG.SW



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

Roche has been very active in the M&A space in 2023 where peers have been more cautious considering potential implications of the IRA. It purchased Televant Holdings, Inc. for $7.25B in addition to Carmot Therapeutics for $3.46B and select assets of LumiraDx for $350M. In addition, Roche continues to invest heavily in in-house R&D efforts with 20 immunotherapy molecules currently in the pipeline. They have also cleaned out underperformers, removing Belvarafenib and RG6286 from costly phase 1 cilinical trials. Although they experienced a decrease in YoY revenues in 2023, they increased gross profit and net income margins over 2022. With exciting new drugs in the pipeline, strong revenue growth potential, and a near mean P/E Roche is a great addition to the ETF.

Novartis AG (SWX: NOVN)

ETF Weight	ADR Price	ADR 1 Yr	NYSE:	Industry	As of:
14.9%	$93.08	(0.13%)	NVS	Healthcare	April 17, 2024

Business Description

Novartis AG engages in the research, development, manufacture, and marketing of healthcare products in Switzerland and internationally. The company offers prescription medicines for patients and physicians. It focuses on therapeutic areas, such as cardiovascular, renal and metabolic, immunology, neuroscience, and oncology, as well as ophthalmology and hematology. Novartis AG has a license and collaboration agreement with Alnylam Pharmaceuticals to develop, manufacture, and commercialize inclisiran, a therapy to reduce LDL cholesterol; and Dawn Health for the development and commercialization of Ekiva, a digital solution designed for people living with Paroxysmal Nocturnal Hemoglobinuria. The company was incorporated in 1996 and is headquartered in Basel, Switzerland.

NOVN Overview

Market Cap: 190.311B
5 Yr Beta: 0.47
Dividend Yield: 4.05%

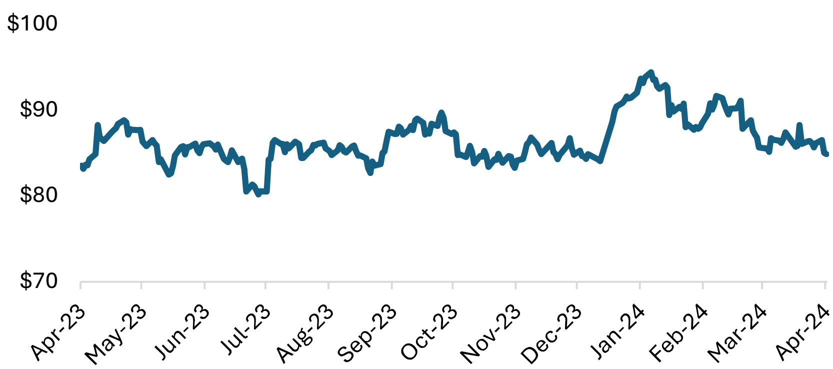
Operating Metrics

YoY Rev Growth: 7.4%
Gross Margins: 74.2%
Profit Margins: 31.8%

Multiples

P/E: 24.93x
EV/Sales: 5.06x
EV/EBITDA: 13.30x

NOVN LTM Stock Performance



NOVN has experienced some volatility in 2023. Following a dip in June due to investor uncertainty of key offerings, their $15B buyback drove prices back within normal range. It has since appreciated due to key acquisitions, but full integrations are yet to be completed.

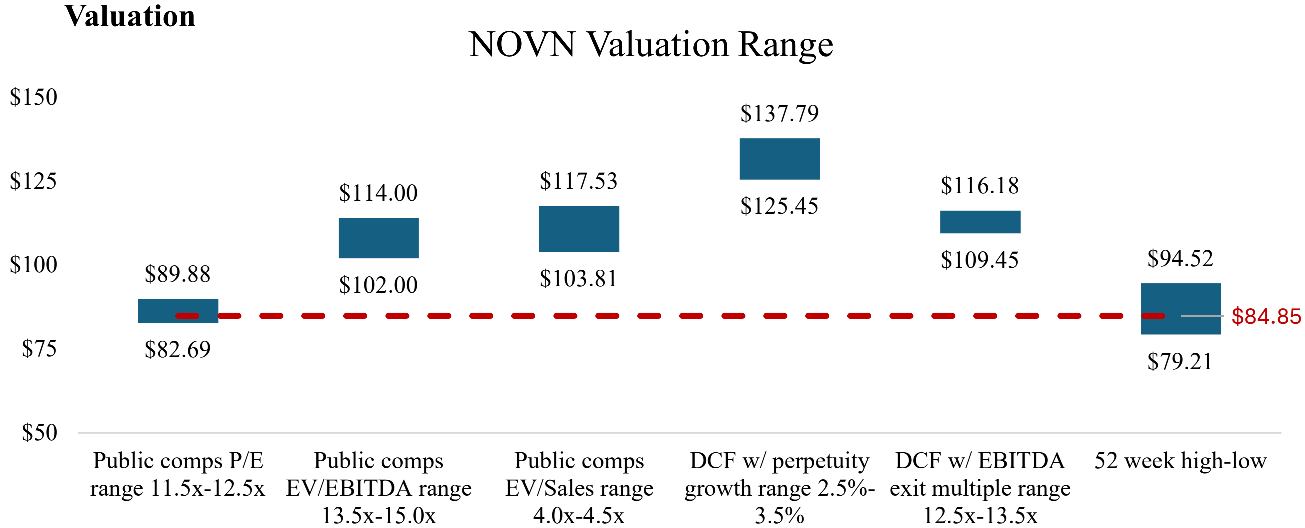
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	13,208		12,092	11,776
2022	12,814		10,783	
2021	12,694	13,294	13,367	13,522
2020	12,708	11,622	12,538	13,030

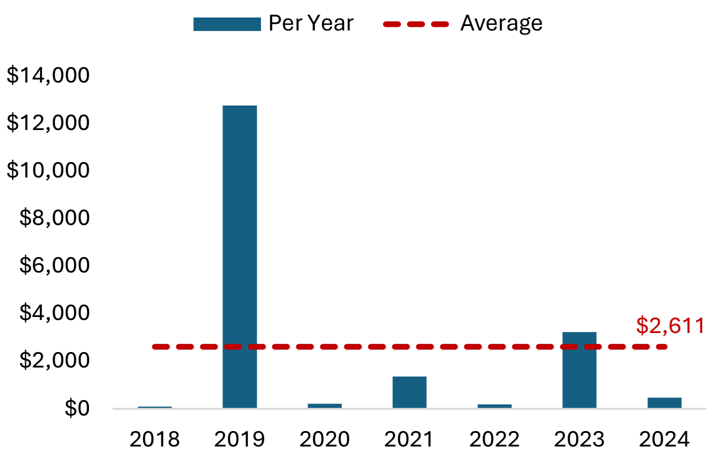
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	1.09		0.85	4.14
2022	1.00		0.73	
2021	0.91	1.29	1.23	7.29
2020	0.96	0.82	0.85	0.92

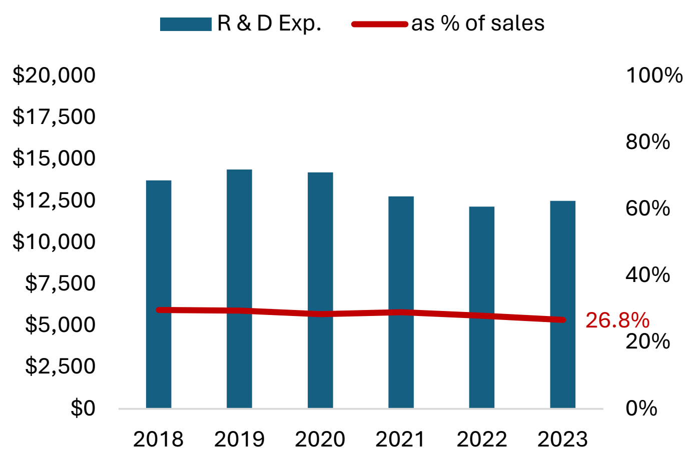
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

Similar to JNJ, Novartis has been in a time of refocus for the past few years. They have gone through with select spin-offs such as their 2019 spin-off of Alcon, their eye care division, and thei 2023 spin-off of Sandoz Group AG, which produces generics and biosimilars. Amid investor uncertainty in June of 2023 Novartis engaged in a buyback of $15B worth of stock. Now, they continue to invest heavily not only on M&A, with new additions such as DTx Pharma, Inc and Chinook Therapeutics, but also in R&D. They are investing heavily in gene therapies via Zolgensma, CAR-T therapies via Kymriah, and targeted protein degradation. Kymriah utilizes groundbreaking CAR-T cell therapy to treat certain types of cancer and has great potential to mimic the success of Perjeta, Tecentriq, and Kisqali.

Bristol-Meyers Squibb

ETF Weight	Price	1 Year Return	NYSE:	Industry	As of:
20.2%	$48.35	(31.52%)	BMY	Healthcare	April 16, 2024

Business Description

Bristol-Myers Squibb Company discovers, develops, licenses, manufactures, markets, distributes, and sells biopharmaceutical products worldwide. It offers products for hematology, oncology, cardiovascular, immunology, fibrotic, and neuroscience diseases. Its main oncological offerings include Yervoy for the treatment of patients with unresectable or metastatic melanoma; Empliciti for the treatment of multiple myeloma; Abecma for the treatment of relapsed or refractory multiple myeloma; and Opdualag for the treatment of unresectable or metastatic melanoma. It sells products to wholesalers, distributors, pharmacies, retailers, hospitals, clinics, and government agencies. The company was formerly known as Bristol-Myers Company. Bristol-Myers Squibb Company was founded in 1887 and is headquartered in Princeton, New Jersey.

BMY Overview

Market Cap:	97.83B
5 Yr Beta:	0.39
Dividend Yield:	4.95%

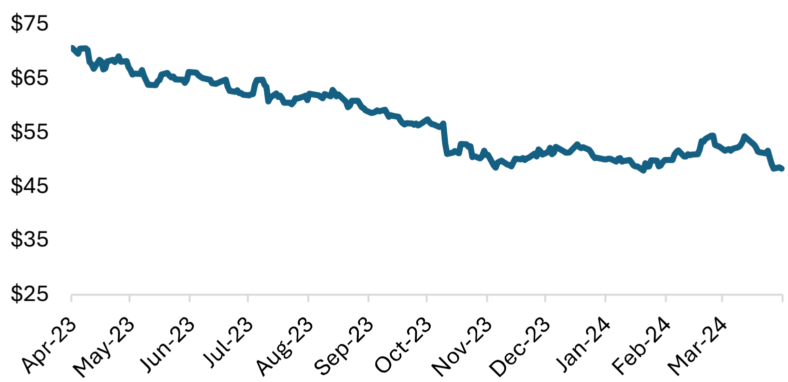
Operating Metrics

YoY Rev Growth:	(2.9%)
Gross Margins:	76.6%
Profit Margins:	17.9%

Multiples

P/E:	13.12x
EV/Sales:	2.92x
EV/EBITDA:	7.00x

BMY LTM Stock Performance



BMY has struggled through 2023 as investors flock to hotter pharmaceuticals companies. In response, BMY made 3 large acquisitions in 2023 which helped stagnate depreciation; however, it is yet to be seen if they achieve optimal integration of new platforms.

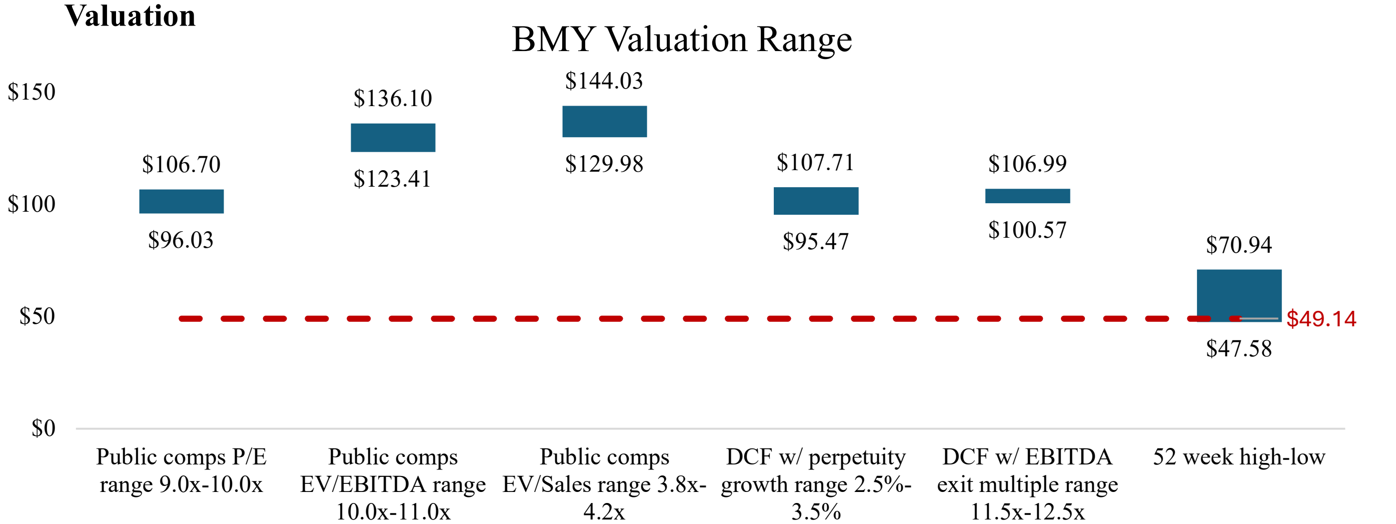
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	11,337	11,226	10,996	11,477
2022	11,648	11,887	11,218	11,406
2021	11,073	11,703	11,624	11,985
2020	10,781	10,129	10,540	11,068

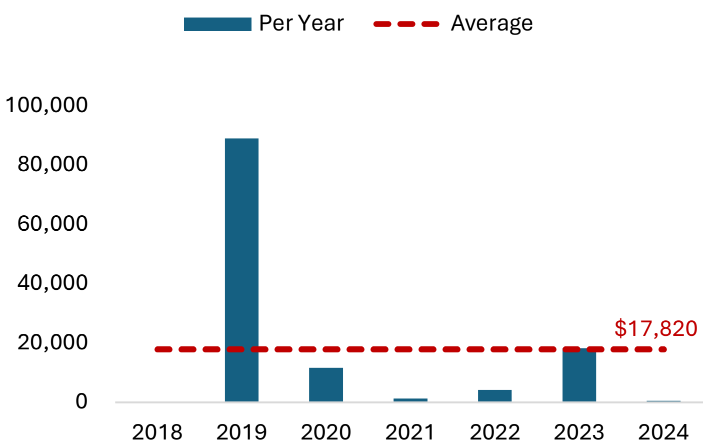
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	1.08	0.99	0.94	0.87
2022	0.60	0.67	0.75	0.96
2021	0.90	0.47	0.70	1.08
2020			0.83	

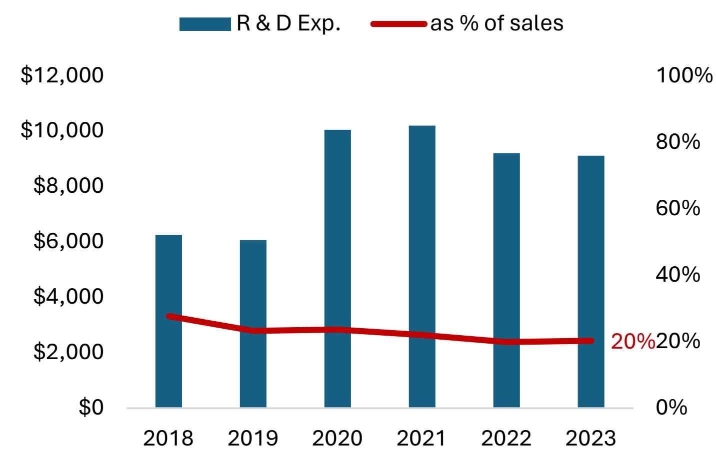
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

While Bristol-Meyers Squibb has dipped roughly 29% in 2023, this is largely due to market sentiment and is separate from their intrinsic worth. Institutional investors worry that BMY's offerings may be outpaced by competitors. In response, BMY announced two large acquisitions in December of 2023: Karuna Therapeutics for $14.025B and RayzeBio, Inc. for $4.152B. Earlier in 2023, BMY also acquired Mirati Therapuetics for $6.053B, making it one of the most active strategics in the pharma M&A market in 2023. These acquisitions will expand offerings in oncology specifically with Mirati having a very promising treatment for non-small cell lung cancer, one of the most deadly cancer types, and a new radiopharmaceutical therapies platform brought in by the RayzeBio acquisition. With a cautious eye on proper integration, they are in an excellent position to thrive in 2024.

Regeneron Pharmaceuticals, Inc.

ETF Weight	Price	1 Year Return	NASDAQ:	Industry	As of:
5.0%	$906.08	8.69%	REGN	Healthcare	April 17, 2024

Business Description

Regeneron Pharmaceuticals, Inc. discovers, invents, develops, manufactures, and commercializes medicines for treating various diseases worldwide. Specifically, it develops product candidates for treating patients with eye, allergic and inflammatory, cardiovascular and metabolic, infectious, and rare diseases; and cancer, pain, and hematologic conditions.

The company's products include EYLEA, myopic choroidal neovascularization, diabetic retinopathy, neovascular glaucoma, and retinopathy of prematurity. Pertinent to oncological offerings, it produces Libtayo to treat metastatic or locally advanced cutaneous squamous cell carcinoma, as well as ZALTRAP for intravenous infusion to treat metastatic colorectal cancer. In addition, the company offers Inmazeb injection for infection caused by Zaire ebolavirus; ARCALYST injection for cryopyrin-associated periodic syndromes, including familial cold auto-inflammatory syndrome and muckle-wells syndrome; and

The company was incorporated in 1988 and is headquartered in Tarrytown, New York.

REGN Overview

Market Cap:	99.416B
5 Yr Beta:	0.14
Dividend Yield:	N/A

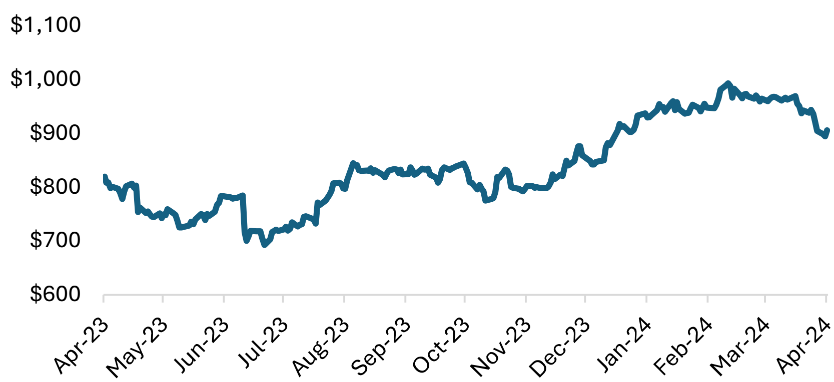
Operating Metrics

YoY Rev Growth:	7.8%
Gross Margins:	52.3%
Profit Margins:	30.1%

Multiples

P/E:	26.82x
EV/Sales:	6.61x
EV/EBITDA:	18.75x

REGN LTM Stock Performance



Following a large negative surprise in Q1, REGN turned investor sentiment with strong Q2 and Q3 performance as it completed its integration of Libatyo and acquired Decibel Therapeutics and 2seventy Bio's R&D pipeline.

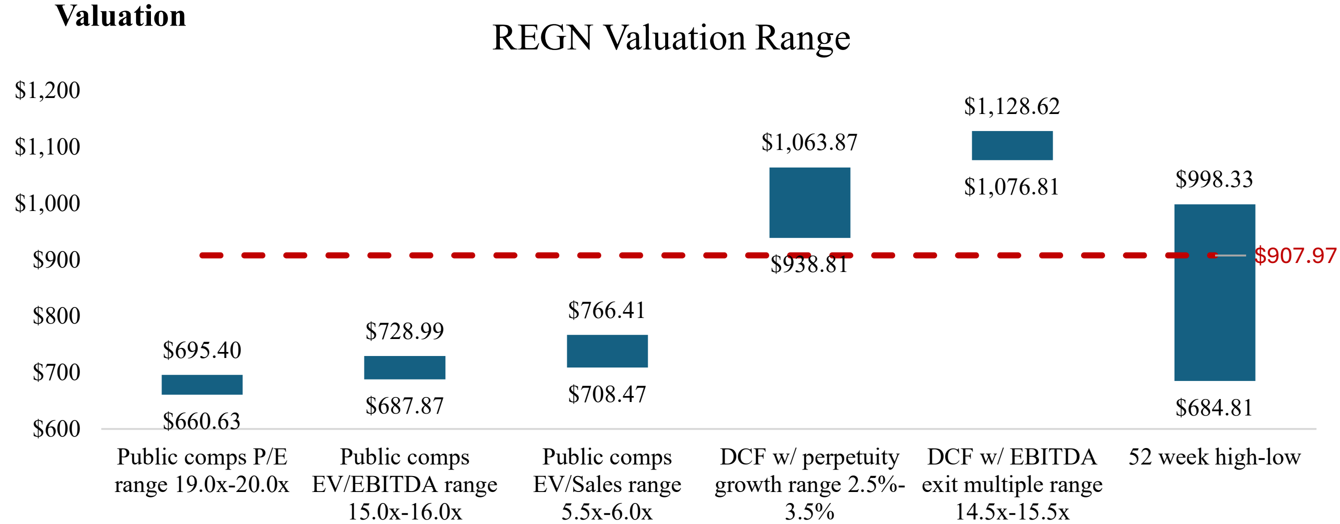
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	3,162	3,158	3,362	3,343
2022	2,965	2,857	2,936	3,414
2021	2,528	5,138	3,452	4,951
2020	1,828	1,952	2,294	2,422

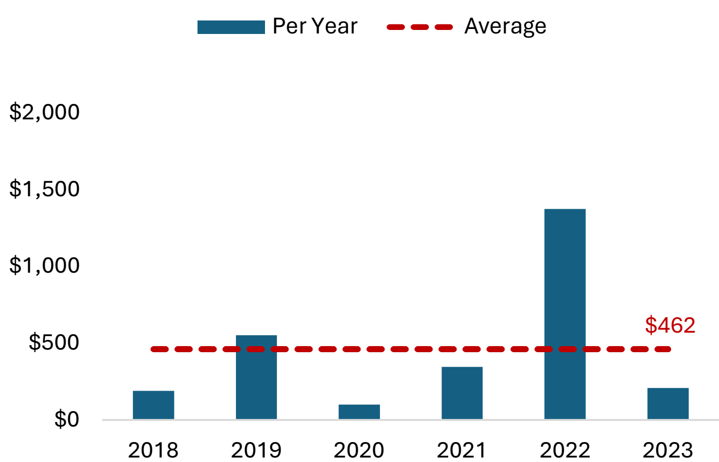
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	7.64	9.05	9.48	10.88
2022	9.12	7.90	12.31	11.19
2021	10.58	29.51	15.37	20.99
2020	5.69	8.19	7.98	10.90

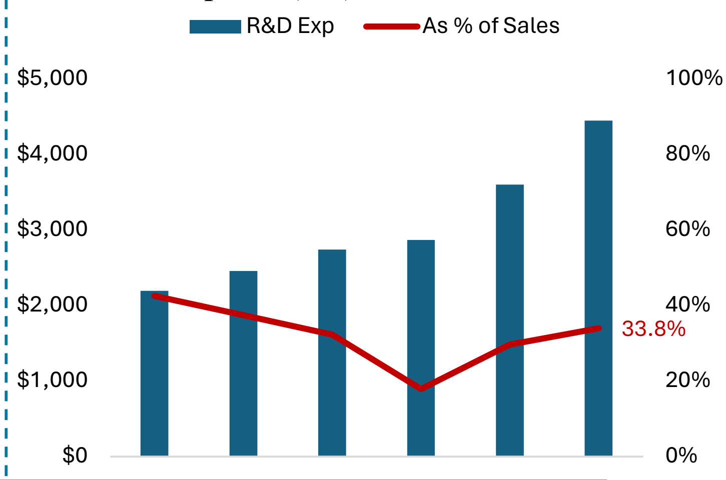
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

While REGN is one of the more expensive stocks in the portfolio, trading at a 26.8x P/E, they are well worth it for their M&A and R&D efforts. They recently acquired exclusive rights to Libatyo in addition to 2seventy Bio's R&D pipeline in order to expand their offerings. Specifically, the 2seventy Bio investigational immune cell therapies are very promising. REGN also continues to invest in in-house R&D with over 30 investigational medicines currently in their pipeline. Though their margins are worse than peer comps, this is largely a tradeoff for their exceptional growth. They have also been one of the more volatile stocks this past year with one of the largest ranges of 52 week high to low.

Gildean Sciences

ETF Weight	Price	1 Year Return	NASDAQ:	Industry	As of:
20.2%	66.95$	(22.71%)	GILD	Healthcare	April 22, 2024

Business Description

Gilead Sciences, Inc., a biopharmaceutical company, discovers, develops, and commercializes medicines in the areas of unmet medical need in the United States, Europe, and internationally. The company provides products for the treatment of HIV/AIDS; Veklury, an injection for intravenous use, for the treatment of COVID-19; and treatments of viral hepatitis. It also offers an oral formulation for the treatment of pulmonary arterial hypertension, and a liposomal formulation for the treatment of serious invasive fungal infections. In regards to oncology, its flagship offerings are currently Yescarta, Tecartus, and Trodelvy.

The company has collaboration agreements with Arcus Biosciences, Inc.; Merck Sharp & Dohme Corp.; Pionyr Immunotherapeutics Inc.; Tizona Therapeutics, Inc.; Galapagos NV; Janssen Sciences Ireland Unlimited Company; Japan Tobacco, Inc.; Dragonfly Therapeutics, Inc.; Arcellx, Inc.; Everest Medicines; Merck & Co, Inc.; Tentarix Biotherapeutics Inc.; and Assembly Biosciences, Inc. It also has research collaboration, option, and license agreement with Merus N.V. for the discovery of novel dual tumor-associated antigens (TAA) targeting trispecific antibodies. The company was founded in 1987 and is headquartered in Foster City, California.

GILD Overview

Market Cap:	83.485B
5 Yr Beta:	0.20
Dividend Yield:	4.61%

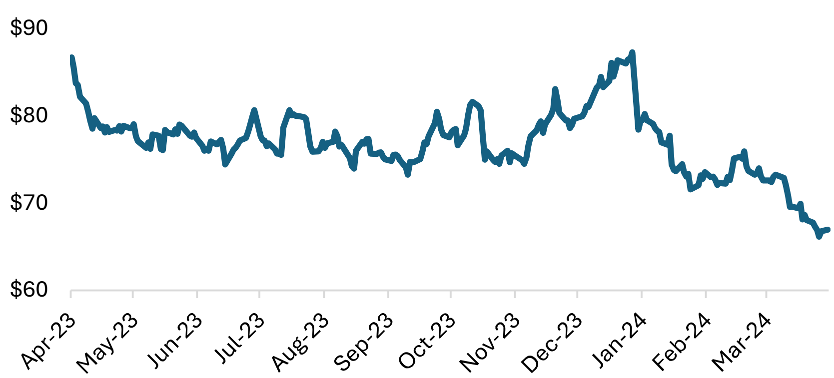
Operating Metrics

YoY Rev Growth:	(0.6%)
Gross Margins:	77.8%
Profit Margins:	20.9%

Multiples

P/E:	15.29x
EV/Sales:	3.76x
EV/EBITDA:	8.05x

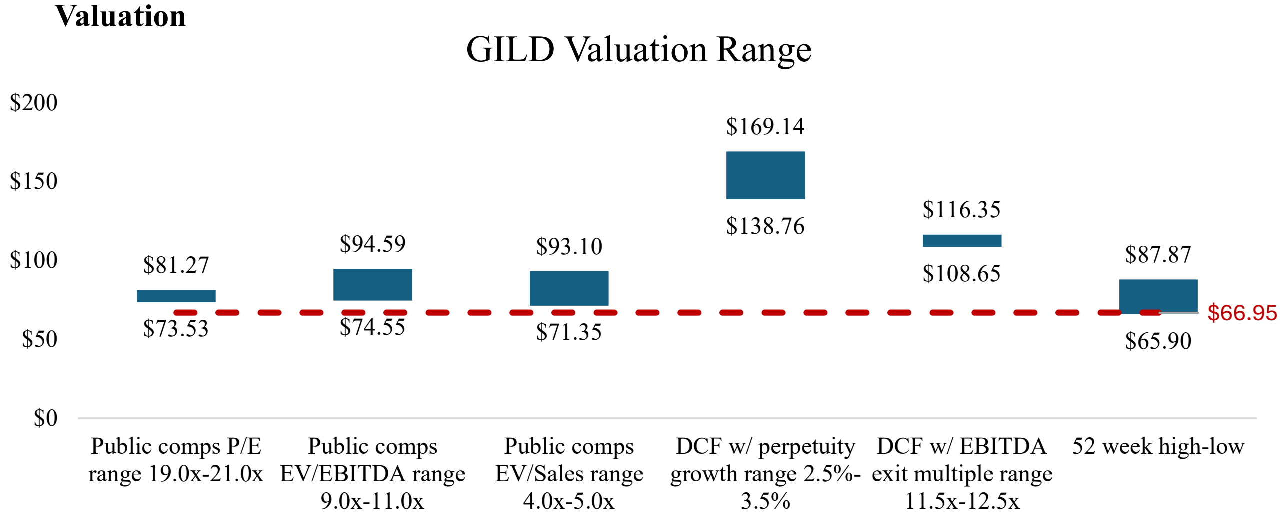
GILD LTM Stock Performance



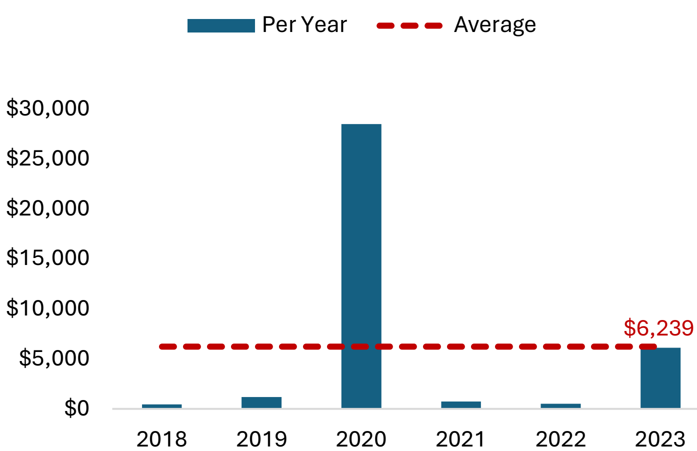
Though GILD experienced volatility following earnings disappointment in Q2 and Q4 of 2023, they have engaged in strategic M&A and R&D to ensure more stable EPS via an expanded portfolio and novel treatments.

	Revenue ($M)				Earnings Per Share			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
2023	6,352	6,599	7,050	7,114	0.81	0.84	1.75	1.15
2022	6,590	6,260	7,042	7,389	0.02	0.91	1.43	1.31
2021	6,423	6,217	7,421	7,244	1.38	1.21	2.06	0.30
2020	5,548	5,143	6,577	7,421	1.23	(2.66)	0.29	1.24

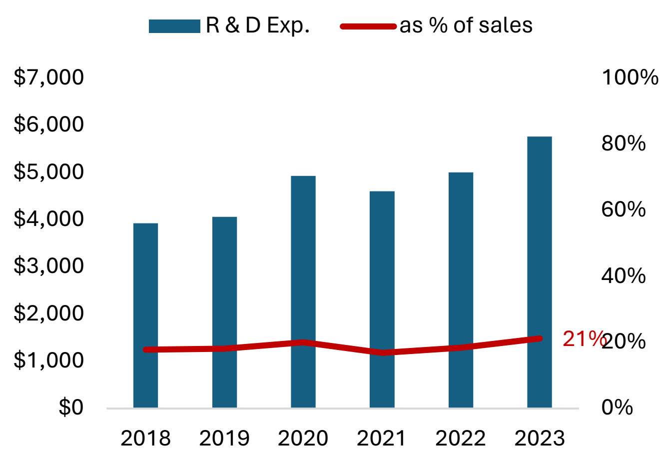
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

Despite top-line stagnation, GILD has experienced expectional growth in its oncological revenues in past years. In 2022 oncological revenues grew 70%, and 37% in 2023. This is in addition to strong growth in sales for their HIVsegment, which is their largest segment. Their oncological sales were largely driven by demand for Trodelvy, their breast cancer treatment, and their cell therapies. GILD also engaged in strategic M&A, acquiring CymaBay Therapeutics for $4.428B and XinThera, LLC for $960M. CymaBay will complement and expand GILD's liver portfolio, potentially leading to best in class treatment for PBC, a chronic liver condition.

Illumina, Inc.

ETF Weight	Price	1 Year Return	NASDAQ:	Industry	As of:
4.7%	$120.25	(47.18%)	ILMN	Healthcare	April 22, 2024

Business Description

Illumina, Inc. offers sequencing- and array-based solutions for genetic and genomic analysis in the United States, Singapore, the United Kingdom, and internationally. It operates through Core Illumina and GRAIL segments. The company offers sequencing and array-based instruments and consumables, which include reagents, flow cells, and library preparation; whole-genome sequencing kits, which sequence entire genomes of various size and complexity; and targeted resequencing kits, which sequence exomes, specific genes, and RNA or other genomic regions of interest. It also provides whole-genome sequencing, genotyping, noninvasive prenatal testing, and product support services; and Galleri, a multi-cancer early detection test. In addition, the company is developing solutions to help accelerate cancer diagnoses, blood-based detection for minimal residual disease, and other post-diagnostic applications. The company serves genomic research centers, academic institutions, government laboratories, and hospitals, as well as pharmaceutical, biotechnology, commercial molecular diagnostic laboratories, and consumer genomics companies. It markets and distributes its products directly to customers, as well as through life-science distributors. Illumina, Inc. was incorporated in 1998 and is based in San Diego, California

ILMN Overview

Market Cap:	19.15B
5 Yr Beta:	1.19
Dividend Yield:	N/A

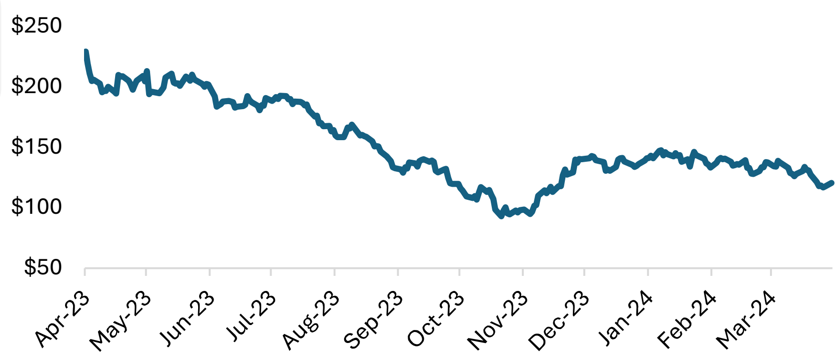
Operating Metrics

YoY Rev Growth:	(1.7%)
Gross Margins:	65.3%
Profit Margins:	(25.8%)

Multiples

NTM P/E:	127.8x
EV/Sales:	4.70x
EV/EBITDA:	45.93x

ILMN LTM Stock Performance



Following a negative Q3 surprise due to a large goodwill impairment, ILMN has recovered slightly and has been range-bound for past months. With

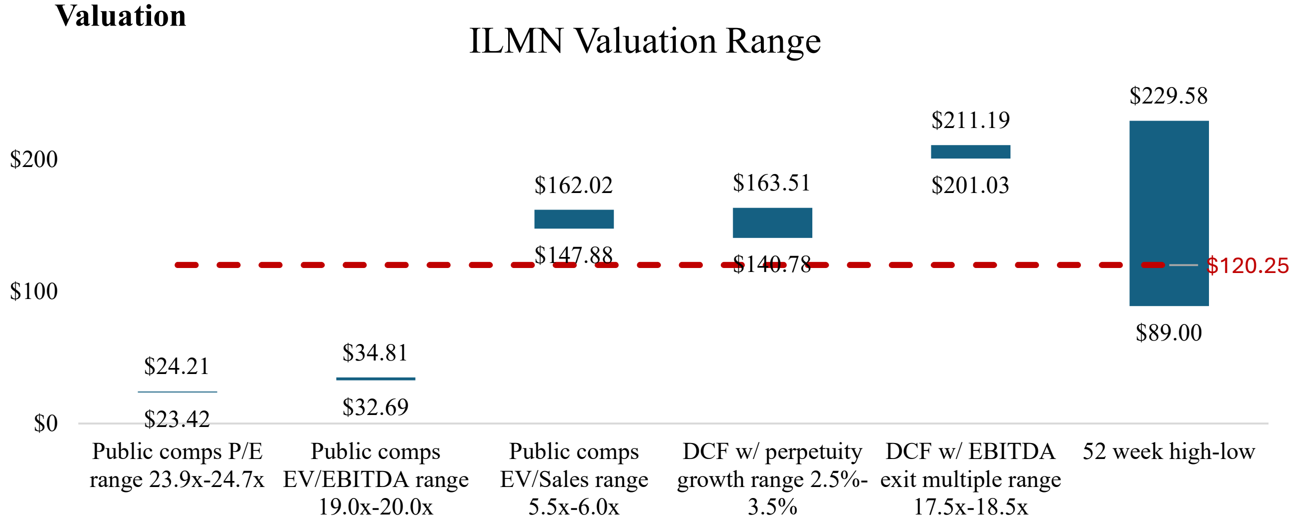
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	1,087	1,176	1,119	1,122
2022	1,233	1,162	1,115	1,083
2021	1,093	1,126	1,108	1,199
2020	859	633	794	953

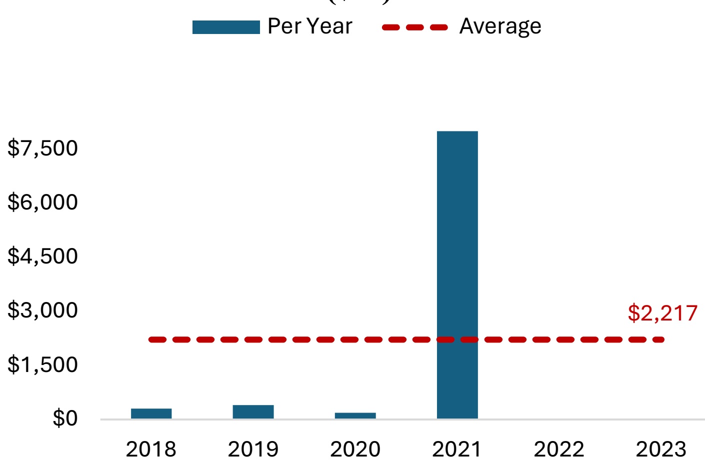
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	0.02	(1.48)	(4.77)	(1.10)
2022	0.55	(3.41)	(24.31)	(0.88)
2021	1.01	1.27	2.09	0.71
2020	1.18	0.32	1.23	1.76

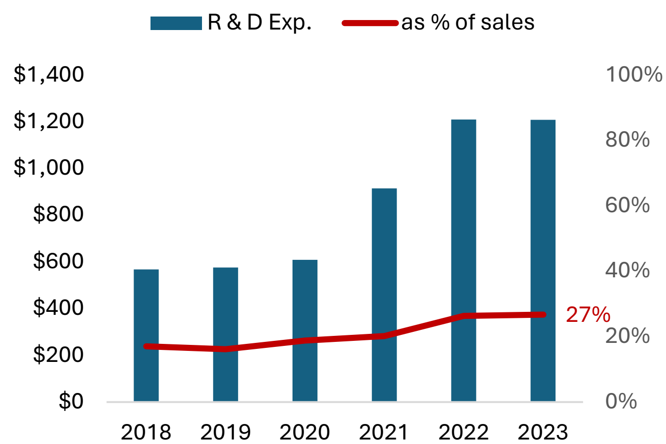
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

ILM is one of the ETF's riskier stocks, with a beta roughly 3x the portfolio's average. Despite their volatility and the worst M&A profile of the portfolio, ILMN's positioning as a best in class genetic sequencing provider covers a key niche in oncological treatment, its detection. In recent years regulatory concerns, goodwill impairment charges, and legal proceedings have made investors more worried due to poor earnings performance. Despite serving a key function in the oncology economy, ILMN will have to prove itself capable of right-sizing operations and recovering EPS performance to turn investor sentiment. Though EPS is expected to turn positive in 2024 and 2025 it will still need strong growth from there. With a strong R&D pipeline and continued genomics leadership, they will hopefully be able to do this; however, they are still one of the least weighted stocks due to this comparative riskiness and uncertainty.

Incyte Corporation

ETF Weight	Price	1 Year Return	NASDAQ:	Industry	As of:
4.9%	51.92$	51.92%	INCY	Healthcare	April 22, 2024

Business Description

Incyte Corporation, a biopharmaceutical company, engages in the discovery, development, and commercialization of therapeutics for hematology/oncology, and inflammation and autoimmunity areas in the United States and internationally. The company offers treatment of intermediate or high-risk myelofibrosis, polycythemia vera, and steroid-refractory acute graft-versus-host disease; treatment for relapsed or refractory diffuse large B-cell lymphoma; a fibroblast growth factor receptor kinase inhibitor that act as oncogenic drivers in liquid and solid tumor types; treatment for chronic myeloid leukemia and Philadelphia-chromosome positive acute lymphoblastic leukemia; and treatment for adults with metastatic or recurrent locally advanced Merkel cell carcinoma, as well as a cream for treatment of atopic dermatitis. It has multiple oncological treatments in Phase 2 and Phase 3 of clinical trials.

It has collaboration out-license agreements with Novartis and Lilly; in-license agreements with Agenus, Merus, MacroGenics, and Syndax; and collaboration and license agreement with China Medical System Holdings Limited. The company sells its products to specialty, retail, and hospital pharmacies, distributors, and wholesalers. The company was formerly known as Incyte Genomics Inc. It was incorporated in 1991 and is headquartered in Wilmington, Delaware.

JNJ Overview

Market Cap:	11.657B
5 Yr Beta:	0.67
Dividend Yield:	N/A

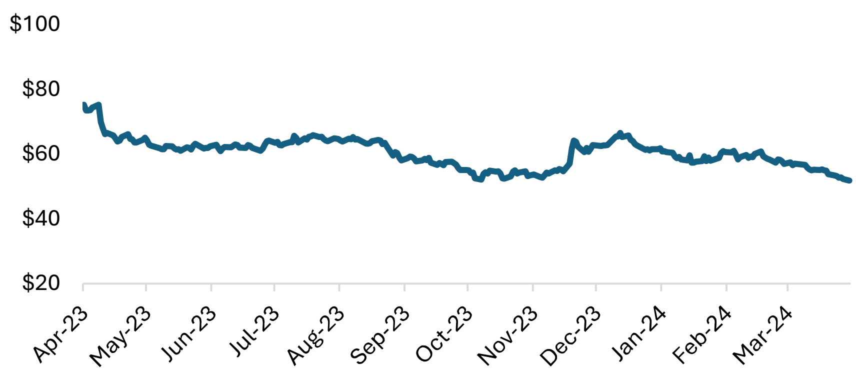
Operating Metrics

YoY Rev Growth:	8.9%
Gross Margins:	49.0%
Profit Margins:	16.2%

Multiples

P/E:	20.49x
EV/Sales:	2.32x
EV/EBITDA:	11.47x

INCY LTM Stock Performance



Despite a promising pipeline complimented by recent acquisitions, INCY has been largely range bound for the LTM period. This is due to neutral investor sentiment as they see INCy's effectiveness in achieving high-impact launches on new offerings.

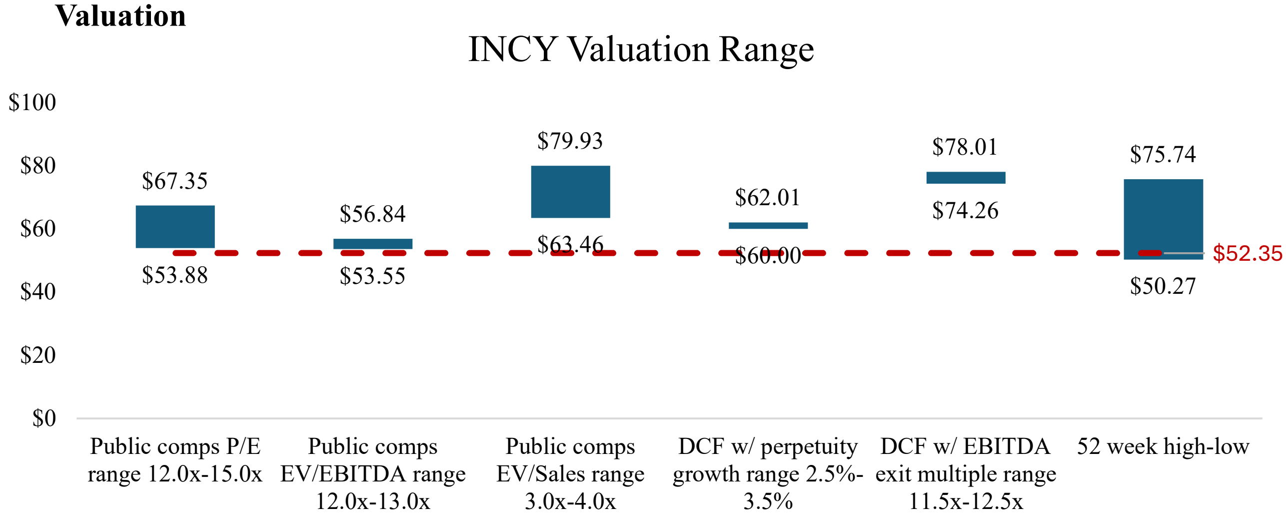
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	808	954	919	1,013
2022	733	911	823	926
2021	604	705	813	862
2020	568	688	620	789

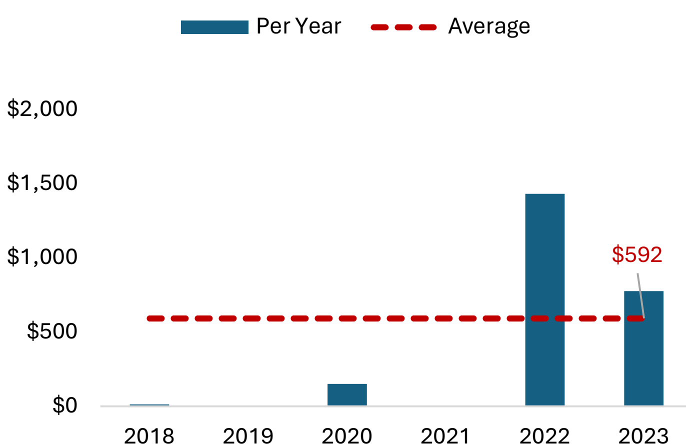
Earnings Per Share

	Q1	Q2	Q3	Q4
2023	0.10	0.91	0.76	0.90
2022	0.17	0.73	0.51	0.13
2021	0.24	0.68	0.82	2.55
2020	(3.33)	1.33	(0.07)	0.68

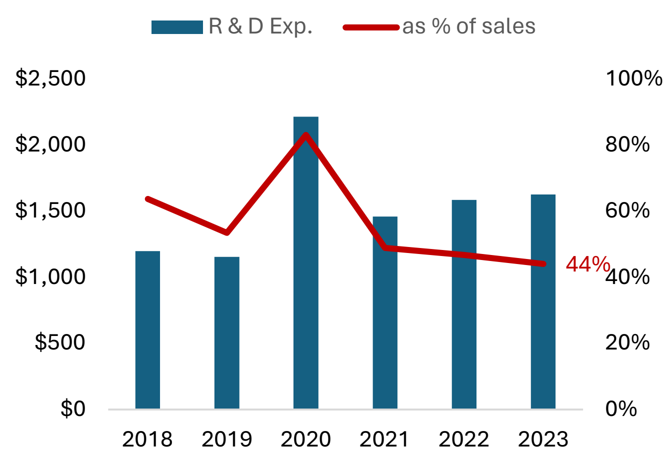
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Investment Rationale

INCY has one of the most promising oncological platforms; however, due to its size disadvantage to larger playes and poor margins it has fairly neutral investor sentiment. They completed their biggest acquisition in 2022 with their $1.43B acquisition of Villaris Therapeutics. In 2024, they have completed two smaller acquisitions: the rights for tafasitamab, a treatment for large B-cell lymphona, for $25M, and Escient Pharmaceuticals for $750M. Escient will help INCY exand into the inflammatory and autoreactive spaces, diversifying and widening its offerings. INCy also has one of the highest R&D levels as a percent of revenue. This focus is spread across oncology, inflamation and autoimmune diseases, and epigenetics research and their set goal is to have 10 high impact releases by 2030.

Passed Investment Example

Johnson & Johnson

ETF Weight	Price	1 Year Return	NYSE:	Industry	As of:
N/A	$144.45	(12.72%)	JNJ	Healthcare	April 16, 2024

Business Description

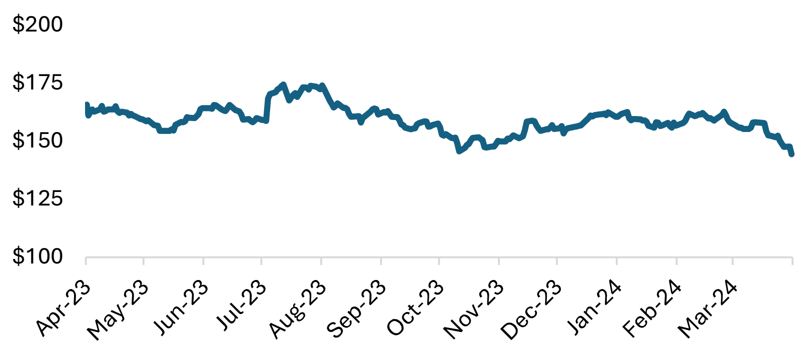
Johnson & Johnson researches, develops, manufactures, and sells pharmaceuticals and medical devices worldwide. Their Innovative Medicine segment offers products for various therapeutic areas, such as immunology, infectious diseases, neuroscience, oncology, cardiovascular and metabolism, and pulmonary hypertension. Its MedTech segment provides Interventional Solutions, including electrophysiology products to treat heart rhythm disorders; the heart recovery portfolio, and neurovascular care that treats hemorrhagic and ischemic stroke. MedTech also offers an orthopedics portfolio, a surgery portfolio, and contact lenses. It distributes its products to wholesalers, hospitals, and retailers, as well as physicians, nurses, hospitals, eye care professionals, and clinics. Johnson & Johnson was founded in 1886 and is based in New Brunswick, New Jersey. In May of 2023, JNJ spun off its consumer healthcare brands such as Aveeno and BandAid, under Kenvue.

JNJ Overview	
Market Cap:	348.093B
5 Yr Beta:	0.53
Dividend Yield:	3.23%

Operating Metrics	
YoY Rev Growth:	6.5%
Gross Margins:	24.0%
Profit Margins:	22.4%

Multiples	
P/E:	14.26x
EV/Sales:	4.37x
EV/EBITDA:	12.03x

JNJ LTM Stock Performance



Following the jump in JNJ stock following its spin off of Kenvue in 2023 it has remained largely stagnant and range bound. Although strategic add-ons have raised EBITDA, EPS performance is still below historical levels and its stock is trading at a discount to peers.

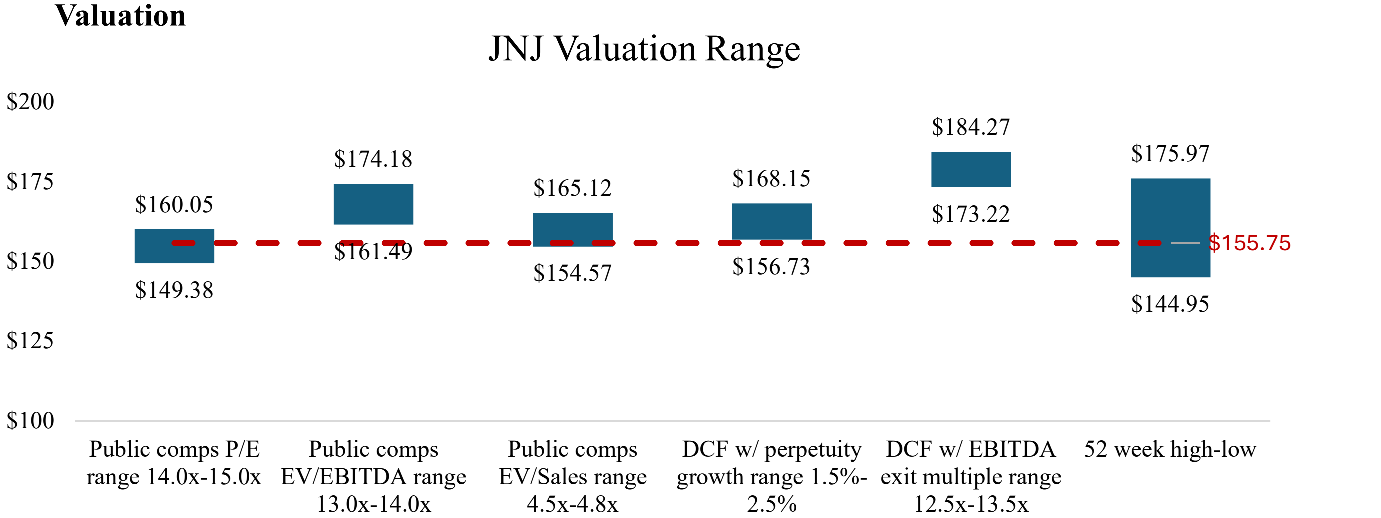
Revenue ($M)

	Q1	Q2	Q3	Q4
2023	24,746		21,3531	21,395
2022	23,426		12,996	
2021	23,312	23,312	23,338	24,804
2020	20,691	18,336	21,082	22,247

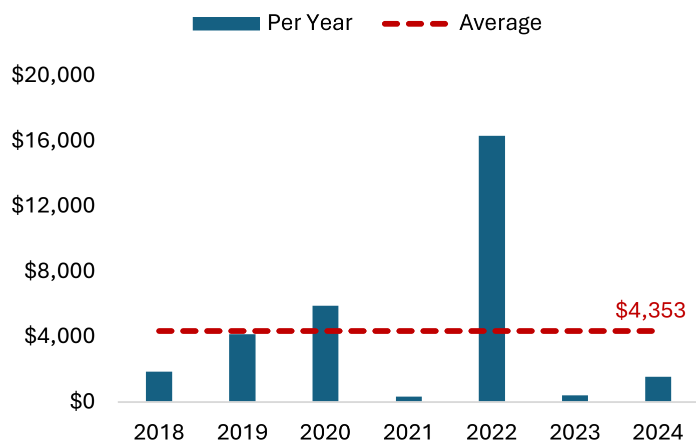
Earnings Per Share

	Q1	Q2	Q3	Q4
2023			1.71	1.49
2022	1.96		1.70	
2021	2.35	2.38	1.39	1.80
2020	2.20	1.38	1.35	0.66

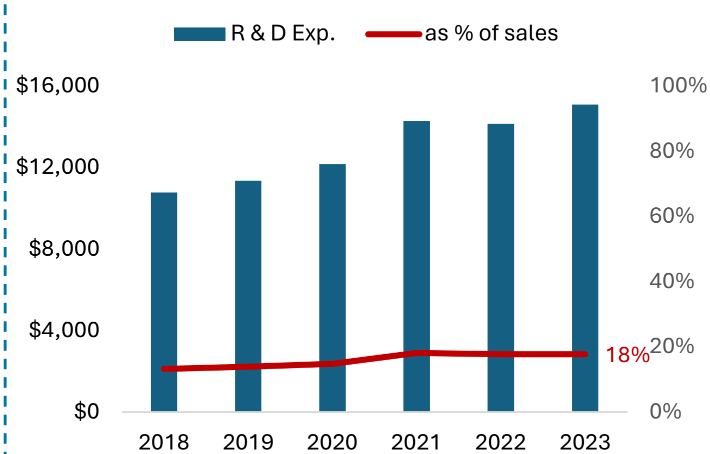
Valuation



YoY Total M&A ($M)



YoY R&D Expense ($M)



Pass Rationale

Althoguh JNJ saw initial appreciation following their split from Kenvue and acquisition of Abiomed, they have since been range bound as investor sentiment waivers. Though they have immense growth potential assuming they can regain market control in their primary operating sectors of pharmaceuticals and MedTech, they have yet to do so. Additionally, there are still structural complications following the Kenvue split. Thoguh they continue to maintain M&A activity – currently they have just completed the acquisition of Ambrx – they also fell short of the ETF's R&D minimum requirement. It could be rationalized to include them in the following months depending on how effective they are at integrating Ambrx into their portfolio; however, unless they show more interest in expanding oncological offerings they are simply too distracted by other markets andoperational segments.

Conclusion

This project was meant to achieve two goals; first, establish an academic basis for the potential of custom SB ETFs, focusing on high growth industries, to achieve alpha for retail traders; second, to exhibit how a retail trader can go about researching, constructing, and quantitatively weighting such an ETF.

Through part one I established the history and investment strategies for the diverse asset class of ETFs. In addition, I established an academic basis for the potential of custom ETFs focused on growth industries to achieve alpha by taking advantage of total market gains while diversifying away unsystematic risk associated with high risk individual securities.

Though my own ETF is much smaller than the necessary amount to diversify away all idiosyncratic risk, this is largely due to the fact that I am investing in a subclass of industry leaders in the oncology economy. While there is no clear singular industry leader, these companies are the most likely to continue consolidating the oncology market via acquisitions and breakthrough R&D efforts. In addition, most of my companies have a much lower historical risk as made evident by the portfolio Beta of .34. These strategics have pharmaceuticals multiple product lines spanning multitudes of diseases. Additionally, some have alternative operating segments focusing on non-pharmaceutical endeavors. These are non-discretionary items that people need without consideration of market conditions. Additionally, with the projected increase in cancer cases means that demand will only increase in the future.

By choosing to systematically weight the portfolio following a Sharpe-optimization strategy, I hope to increase total alpha by investing more in the companies with the best risk-to-reward. Overall, the predicted Sharpe ratio is very promising. Although estimated Sharpe may be somewhat inflated at 4.17 and annual returns will not be as consistent as projected, I believe the portfolio to have an excellent chance of achieving above average risk-weighted returns. Continued monitoring, including investment in new, promising companies and divestiture of underperforming assets, will be necessary to achieve this return. However, this process will take place over many years and for now I believe the portfolio to be excellently positioned to take advantage of the projected 16% annual growth of the oncology economy.

Next Steps

Through this paper I have hoped to exhibit the plausibility of retail traders utilizing custom ETFs to gain exposure to high growth markets. However, due to time constraints I have not been able to track actual results. Next steps will thus be to track and analyze risk-adjusted returns quarterly. Additionally, with the breakneck pace of innovation, it is plausible holdings will need to be expanded or trimmed accordingly.

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