Artisan Partners Global Equity Team

# Pipelines for Resilient Growth

Resilient Growth

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When it comes to finding resilient growth in biopharma, Research Analyst Navdeep ("Nav") Singh of the Artisan Partners Global Equity Team takes a consistent approach to an often-volatile sector allowing the team to produce positive results for the portfolio and its investors.

**Navdeep ("Nav") Singh**
Research Analyst

## From Pandemic Travel to Implementing the Checklist

Nav has a background in biology and economics with almost 18 years of experience researching biopharma companies, first at Goldman Sachs and then at Fidelity. Nav first met Portfolio Manager Mark Yockey during the darkest days of the global pandemic. In fact, Nav's flight from Boston to San Francisco to interview with Mark was one of the first flights that opened up to a handful of brave passengers who boarded planes armed with N95 masks, gloves and Clorox wipes and after initial lockdown orders grounded the airlines in 2020. Nav survived the journey in good order and returned with an opportunity to not only expand his coverage to include a wider number of subsectors in health care, but also to work with someone as passionate and knowledgeable about the sector as he was. The two discovered that they shared the view that health care is a special sector given its capability of making a difference in people's lives while generating long-term investment growth for investors. After Nav joined Artisan Partners, he quickly became known as the "COVID analyst" on the team. However, as all of the analysts soon discovered, everyone would become de-facto COVID analysts given that the pandemic materially affected just about every company across sector and region in a profound way.

One of the first things Nav did upon joining the team was to implement a framework for researching health care companies. It was a checklist, of sorts, for those qualities a company must demonstrate to him and the team before they would consider it a candidate for investment. First, the company's key product or innovation must provide a strong benefit to the patient. In Nav's considerable experience, if a drug materially improves quality of life or life expectancy, then it leads to fast adoption and durable use, providing a long runway for growth. Second, the drug must offer the best solution in the market. While often profitable, "me too" drugs are normally not sufficiently differentiated to provide the kind of large market opportunity and catalyst for earnings growth needed to make an investment worthwhile. This leads to the third quality, namely, that the company must have strong research and development capabilities. Over the years, Nav has discovered that R&D is a linchpin capital investment that can unlock ongoing product innovation and make the company and its stock more resilient. And finally, if the first three qualities are present, then the fourth quality can usually be found as well: pricing power. Nav explains further, "This is especially the case if the drug is making a material impact on someone's life."

## Avoiding Binary Risk

One of the largest risks in investing in health care is the binary risk that investors face when a company releases new data on a drug, or a drug goes under FDA review. If the trial goes well and the data is positive, investors will

likely see the company's stock price soar. However, if the trial goes poorly and the data shows the drug to be ineffective, then the stock price sinks, taking investor capital with it. Complicating the scenario is the fact that many variables can affect the outcome of a trial, making it very difficult to predict the results ahead of the binary event.

The team's approach is to first establish proof of concept and then try to de-risk the investment process through in-depth knowledge and proper timing. Nav stresses the importance of establishing some type of confirmation that the formulation reacts positively in a human subject, for instance. Then, he and the team conduct a deep dive into all available data for the drug candidate. They talk with doctors, and may even conduct surveys with them, to understand their attitudes about the drug should it have a positive outcome in the trial. Nav and the team will also speak with the company's management team to understand their plans and vision for launching and marketing the drug. These qualitative factors are quantified in a proprietary valuation model that Nav and others build before the trial.

Once the clinical trial results are released, Nav and the team value the stock given all of the known inputs and stand ready to buy it if the price falls below their target value. By waiting until after the trial to purchase shares, they might miss some of the upside potential of the stock, but they attempt to capture as much of it as they can and are able to do so with much greater certainty than if they had invested before the binary event. More importantly, they will not commit investor capital until they have a solid understanding of the stock's valuation, usually after the data readout of a stage 2 or 3 clinical trial.

Nav currently sees several areas in health care that he believes represent resilient growth opportunities for the Artisan International Fund and Artisan Global Equity Fund.

## Obesity

With more than $33 billion in annual revenues, Novo Nordisk is a well-managed company with a strong R&D capability that dominates the diabetes market, which is growing around 12% per year. In chronic weight management, Novo Nordisk is leading the way with Wegovy, a semaglutide-based drug that is associated with Ozempic, a type 2 diabetes treatment. It has been approved for use across North America and Europe and is part of a class of drugs that mimics a natural hormone in the brain to get the pancreas to release insulin. It also helps control appetite and by slowing the processing of food in the stomach.

"In biopharma, we are investing in some of the biggest trends going on right now."

With more than half of the adult population in the US and Europe currently considered either overweight or obese, the total addressable market for Wegovy is undeniably large. The treatment has been proven to be safe and effective and is leading patients to lose up to 15% of their body weight in one year.

In addition, the company announced the launch of a phase 3 trial for a drug candidate called CagriSema which uses a combination of cagrilintide and semaglutide to treat type 2 diabetes and has shown even greater weight reduction benefits for overweight and obese subjects. Obesity, in particular, is linked with increased cardiovascular disease, cancer and type 2 diabetes. Last year, the company produced data showing Wegovy cut the risk of heart disease by 20% and is currently seeking a label expansion with this claim. If successful, it would be an important differentiator for the drug over other weight management drugs. Thus, Novo Nordisk is currently trying to establish a link between Wegovy use and longevity among obese patients. Establishing this link would further solidify the benefits of this drug and help change the medical community's views on obesity from being a primarily behavioral issue to being a physiological, and now treatable, medical condition.

For the company, this new drug platform, often referred to by Nav as a pipeline within a drug, represents a source of recurring revenue for years to come. In Nav's view, Wegovy builds on the company's already strong line of treatments in type 2 diabetes that has been on the market for years and bolsters Novo Nordisk's credentials as a durable grower. He adds, "Novo has a great lineup of innovative drugs that lack any immediate patent cliffs." A patent cliff is when a drug comes off a patent and faces competition from generic drug makers, normally driving the price and profits down dramatically.

In January this year, Lilly, a direct competitor to Novo Nordisk in diabetes and obesity, launched Zepbound in the US. It uses tirzepatide, a different type of GLP-1 in its drug. Analysts expect Lilly to reach $2 billion in sales in 2024. For Novo Nordisk, Nav is counting on Wegovy's patent sunsetting while CagriSema continues under longer-dated patent protection, in effect extending the value of the intellectual property underlying franchise. Nav and the team believe the market for this type of drug could unlock a $50 billion opportunity for the players.

"That's what investors want," Nav explains. "A long revenue stream from a particular innovation."

## Cancer

Nav recently worked with Mark and the team to add Japanese drug maker Daiichi Sankyo on their strong conviction in its line of antibody drug conjugates (ADCs). ADCs deliver chemotherapy agents directly to cancer cells making these powerful chemicals both more effective and less damaging to healthy cells surrounding the cancer. The company has three drug treatments in this class that are either on the market or in testing.

In the breast cancer treatment space, Daiichi Sankyo has a 50/50 partnership with AstraZeneca to produce an ADC with the trade name of Enhertu. Enhertu is quickly becoming the new standard of care for patients with a type of cancer that grows and spreads quickly and currently represents about 70% of all cases. The drug was approved by the FDA in 2019 and is already improving life expectancy in patients. With a high degree of confidence in the drug's future success, Nav believes sales of Enhertu will grow revenues to around $12 billion globally. He views Enhertu as a product that provides "downside protection" as Daiichi Sankyo develops other drug candidates.

"ADCs will likely play a really big role in how cancer is treated."

Daiichi Sankyo has another 50/50 partnership with AstraZeneca to develop Dato-DXd to treat patients with non-small cell lung cancer. In a phase 3 trial in non-small cell lung cancer patients, Dato-DXd provided a clinically meaningful benefit versus chemotherapy in a large subgroup, which represents 70% of the total population. Based on these encouraging results, Nav believes Dato-DXd will receive FDA approval for the subgroup of non-small cell lung cancer patients by the end of 2024. He thinks Dato-DXd could eventually generate upwards of $10 billion in annual revenues across multiple cancers.

HER3 ADC is solely owned by Daiichi Sankyo and is being developed to treat EGFR lung cancer, a type of mutating cancer that occurs in about 10% to 15% of patients and is more common among younger ones. To date, the company has produced encouraging data showing good response rates and is currently awaiting priority review by the Food and Drug Administration and possible US approval in mid-2024. Nav estimates that HER3 could be a $2.5 billion drug in the US, Europe and Japan.

Lastly, Daiichi Sankyo entered into a lucrative 50/50 partnership with Merck to develop and commercialize three additional ADCs outside of Japan that target EGFR+ lung cancer, small cell lung cancer and ovarian cancer. The agreement gives Daiichi Sankyo the potential to earn 50% of profits, up to $22 billion, in milestone payments and reimbursements with Merck covering a significant portion of R&D costs. Best of all, with experience in pioneering top-selling cancer treatment Keytruda, Merck represents a partner that can help accelerate the development and distribution of these ADCs, allowing them to achieve their full sales potential.

With an R&D unit producing highly-targeted life-saving drugs that change how cancer is treated, Daiichi Sankyo is another example of a company that fits Nav's checklist. Nav believes the company has the potential to leverage its baseline research to develop a powerful pipeline with a high likelihood of future success.

## Autoimmune Disease

It is estimated that as many as 4.5% of the world's population is affected by an autoimmune disease, a condition in which the body's immune system, designed to protect the body by fighting germs and other harmful substances that enter the body, instead turns against itself and attacks healthy cells. In the US, about 10 million people suffer from autoimmune diseases such as multiple sclerosis and rheumatoid arthritis.

Argenx, a biotech company that develops therapies for severe autoimmune diseases, was first added to the portfolios by the team in 2021. Its most important drug, Vyvgart, is an advanced treatment option for patients with generalized myasthenia gravis (gMG), a rare and chronic autoimmune disease that causes debilitating muscle weakness. Vyvgart is the most effective FDA-approved treatment for adults with gMG. By destroying and removing harmful antibodies, Vyvgart can help reduce the disruption between the nerves and the muscles, and the debilitating symptoms can be markedly reduced. Vyvgart has been on the market for over two years and has generated about $400 million in revenues. According to Nav, it has the potential of reaching $3.5 billion in several years for treating gMG alone.

Above and beyond having developed an innovative drug for a terrible disease, what Nav likes about Argenx is the opportunity it has to leverage this intellectual property across multiple diseases. He mentions two others, "Vyvgard showed positive phase 3 data for treating idiopathic thrombocytopenic purpura (ITP), a condition that occurs when the immune system mistakenly attacks platelets or when the body doesn't make enough platelets." Platelets are blood cells that form blood clots to help stop bruising and bleeding. Another condition that Nav cites is chronic inflammatory demyelinating polyneuropathy (CIDP). CIDP is a neurological disorder that results in progressive weakness and reduced senses in the arms and legs due to damage to the fat-based protective covering on nerves. Although Nav is waiting on more data regarding the ability of Vyvgard to treat these diseases, he remains optimistic. If Vyvgard is approved for treating ITP and CIDP, then Argenx could be looking at addressing the needs of two additional markets with an additional $4.5 billion in total revenues. This is a perfect example of a *pipeline in a drug*.

"How many more diseases will Vyvgard work in? Argenx has plans to evaluate it in at least 15 more."

"We like this space because sometimes mechanisms like this can act across multiple diseases." He elaborates, "When investors have a line of sight for that much money with these drugs, the increase in stock price could take Argenx from being a mid-cap to a large-cap company."

**Exhibit 1**

| SUBSECTOR | DESCRIPTION | RISK PROFILE | EXAMPLES | FY1 EBITDA MARGIN |
|---|---|---|---|---|
| Large Pharmaceutical or Biopharma Companies | Researches, develops, and markets organic or chemical drugs | Moderate, clinical risk | Novo Nordisk | 48.2% |
| Small Biotech Companies | Primarily focused on advanced research and developing new treatments | High, clinical risk | Argenx | -25.2% |
| Medical Technology (MedTech) | Connects patient care with technology, including medical devices | Low, some clinical risk | Stryker | 26.3% |
| Life Sciences Tools & Equipment | Provides equipment to pharmaceutical companies | Low, no clinical risk | Thermo Fisher Scientific | 25.0% |
| Contract Development and Manufacturing (CDMO) or Contract Manufacturing Organizations (CMO) | Provides development and manufacturing infrastructure to pharmaceutical companies | Low, no clinical risk | Lonza Group | 29.6% |

FactSet 31 Dec 2023.

## Health Care Industry Structure

The health care sector is comprised of several subsectors, each with its own investment profile. Pharmaceutical companies are those using artificial or chemical sources to make drugs. Those companies or divisions that derive products from the extraction or manipulation of living organisms are considered to be biopharmaceutical or biopharma companies. Biotech is a subset of biopharma and consists of smaller, innovative companies that are primarily engaged in development.

As shown in Exhibit 1, large pharmaceutical and biopharma companies—global drug companies with market caps in hundreds of billions of dollars—generally have less business and market risk associated with them than smaller, more innovative biotech firms, which have higher revenue exposure to early-stage drug candidates. Often, small biotech companies are prone to large swings in revenues—from potentially having no revenue to generating significant revenue if a new breakthrough drug achieves commercial success, and their often-volatile stock prices reflect this fact. Nevertheless, both big pharma and small biotech companies face clinical risk, the risk that an experimental treatment may fail to produce the desired medical outcome.

Medical technology companies, or "medtech," generally have lower risk associated with their cashflows than pharmaceutical or biopharma companies. While some medtech companies have high product design and development costs and must perform pre-market and post-market clinical trials, they generally face lower failure risks than do pharma and biopharma drug makers. Nav has found, however, that many of these companies lack the pricing power that the larger drug companies have.

Finally, life sciences and contract manufacturing organizations often offer investors steady growth within health care without clinical risk. Many of these companies provide the tools and services—from lab equipment to running a drug company's clinical trials—that are necessary for the industry to function properly.

The health care industry was severely tested during the pandemic, and it proved to be resilient as players from all parts of the ecosystem worked together to quickly develop new vaccines, test equipment and run trials needed to rise to the challenge. In the end, each of these areas played a critical role in the fast response to COVID-19, and many people benefited from new knowledge and capabilities gained in the process. In fact, in many ways, the response to COVID-19 showed the world the immense power of innovation within the health care industry. This was highlighted by the industry developing and deploying a vaccine within one year of the initial outbreak, an unprecedented response.

## The Long War

In January 1971, President Richard Nixon launched a war on cancer, which had become the second-leading cause of death in the United States, by asking for an appropriation of $100 million during his State of the Union Address to Congress. More than half a century and billions of dollars later, the war on cancer still rages on. To be fair, important battles have been won along the way. Mortality rates from cancer have shrunk greatly, and the number of survivors continues to grow, mainly from improved screening, detection, prevention and treatment.

Progress in medicine often happens slowly, over time, by winning many little battles. It is in this context that the battles against obesity, cancer, autoimmune disease and hundreds of other types of disease often involve developing resilient pipelines and pipelines within drugs that can continue to deliver innovative new treatments for years to come. This type of resiliency eventually wins wars—and it's what drives Nav's unfaltering interest in health care investing every day.

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**Carefully consider the Fund's investment objective, risks and charges and expenses. This and other important information is contained in the Fund's prospectus and summary prospectus, which can be obtained by calling 800.344.1770. Read carefully before investing.**

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This summary represents the views of the portfolio managers as of 31 Mar 2024. Those views may change, and the Fund disclaims any obligation to advise investors of such changes. For the purpose of determining the Fund's holdings, securities of the same issuer are aggregated to determine the weight in the Fund. The holdings mentioned above comprised the following percentages of the Fund's total net assets as of 31 Mar 2024: Artisan International Fund— Novo Nordisk A/S 5.5%, Daiichi Sankyo Co Ltd 1.6%, AstraZeneca PLC 1.0% and Argenx SE 2.2%. Artisan Global Equity Fund: Novo Nordisk A/S 5.0% and Stryker Corp 1.4%. Portfolio holdings are subject to change without notice and are not intended as recommendations of individual securities.

**EBITDA Margin (Earnings Before Interest Tax and Depreciation)** is a measure of a company's operating profit as a percentage of its revenue.

**FY1** is the current forecast year.

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A R T I S A N P A R T N E R S

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