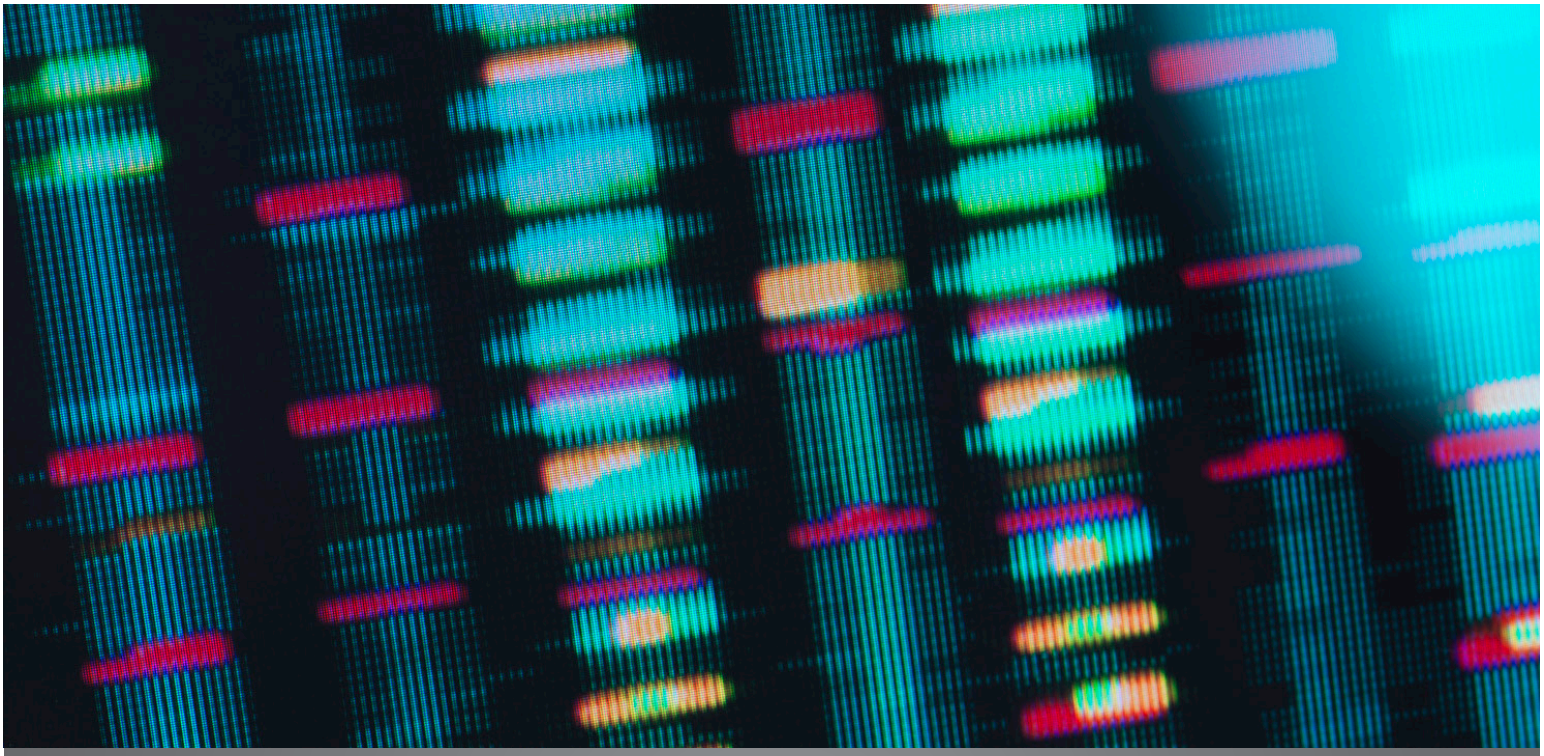


Where We Are Finding Growth

Health Care Innovation

ARTISAN PARTNERS

Insights

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

Where We Are Finding Growth

Artisan Partners Growth Team is committed to finding accelerating profit cycles around the world and investing in reasonably valued companies that are positioned for long-term growth. The team's experience and broad knowledge of the global economy are key attributes that help them identify growth opportunities, wherever they occur, for the four portfolios it manages—Artisan Global Opportunities Fund, Artisan Global Discovery Fund, Artisan Mid Cap Fund and Artisan Small Cap Fund.

Currently, the team has identified a number of compelling secular trends that it believes are catalysts for profit acceleration and that will drive growth for some time to come. In this article, the team discusses one of those trends—health care innovation.

Advances In Human Biology

In the six-plus decades since Francis Crick and James Watson published their short but revelatory article about DNA's double-helix structure, ongoing research has accelerated understanding of human genetics.

That acceleration continues today. The human genome was first fully mapped in 2003—after 13 years and a cost of $2.7 billion. By 2007, the cost required to sequence DNA's roughly 3 billion molecular pairs had collapsed to a mere $1 million. As of 2012, genome sequencing ran $10,000. As 2013 ended, a dominant gene-sequencing and analysis systems player announced it had achieved the $1,000 genome—the biologic equivalent of breaking the sound barrier. Researchers have now set their sights on a 15-minute, $100 test.

A Bigger Discovery and Therapy Toolkit

The increased speed and ease of sequencing DNA has allowed vastly expanded awareness of how genetic code gets translated into the biology of our bodies—and what causes disease. That has opened the door to an ever-growing toolkit of both discovery and therapy delivery which has contributed to a material shift in the pharmaceutical industry—the rising prominence of biologic drugs.

Biologics are large-molecule drugs, typically based on naturally occurring proteins or optimized versions of proteins with some therapeutic effect. The first genetically engineered biologic drug—human insulin for diabetics called Humulin®—was FDA-approved in 1982. Prior, pharmaceuticals were near exclusively chemically manufactured, small-molecule compounds. Though lab methods have improved vastly over time, discovery of traditional pharmaceuticals and their function is still largely the same, often lengthy, process of trial and error—even mere happenstance. (The discovery of penicillin's effectiveness against bacteria was famously serendipitous.)

As opposed to trial and error, biologics are rationally designed. They are based on naturally occurring proteins performing targeted functions with outcomes that, in most cases, have already been observed. Therefore, their effect can be reasonably well understood ahead of time.

Nature's experiments yielding rational designs

Rational design of drugs can yield myriad benefits, like more effective, less toxic therapies yielding better outcomes in clinical trials due to fewer unanticipated adverse events, and condensed approval periods.

For example, several years ago, researchers observed that a small subset of the population had very low, exceptionally healthy levels of LDL cholesterol (i.e., the "bad" cholesterol). Researchers then discovered this population shared a specific trait—a small genetic mutation blocking production of a certain enzyme (PCSK9).

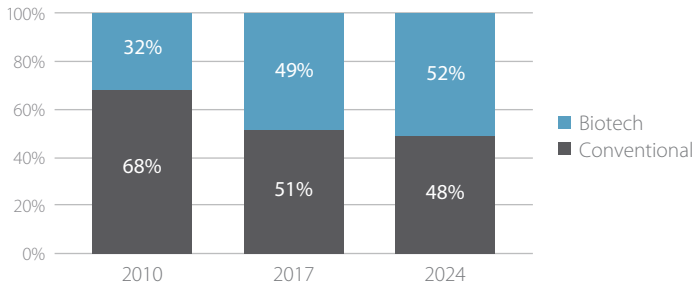
Nature did the experiment—demonstrating the desirable outcome if the PCSK9 enzyme is blocked—allowing researchers to understand reasonably well how to effect it. Now, several biotechnology firms are successfully testing monoclonal antibodies—a class of biologic drugs that mimics natural antibodies to harness the power of the human immune system—to block PCSK9 in populations with very high cholesterol.

The original scientific papers highlighting findings on PCSK9 were published in 2006, and by the end of 2015, the FDA had approved two anti-PCSK9 drugs. To have a new drug approved within nine years—and just five years after pharmaceutical firms selected drug candidates to test—is fairly unprecedented and a promising sign of a new era of precision medicine.

The biologic drug era

The rise of biologic drugs is already changing the marketplace. In 2006, just 21% of top 100 drug sales were biologics. That jumped to 49% in 2016, and by some estimates should reach 52% in 2022 (see Exhibit 1). The runway here is potentially massive.

Exhibit 1: Biotech's Growing Share of Top 100 Drugs



Source: EvaluatePharma estimates of worldwide prescription and OTC pharmaceutical sales, as of June 2018.

The Emergence of RNAi

There are likely still many exciting developments to come in the biologics field. We are also seeing promising developments in the development of novel small molecule drugs, particularly in the area of oncology.

And there are other, potentially ground-breaking new biopharmaceutical medicines still in very early stages. One example is the emergence of RNA-interference (RNAi). When discussing RNAi, we generally refer to two key platforms—RNAi and antisense. Though functioning somewhat differently, RNAi and antisense therapies both effectively and potently target the source of disease-causing enzymes or mutations. This stands in contrast to more traditional pharmaceuticals which were designed to target certain disease-causing enzymes, but only after those enzymes have been produced.

The appeal of next-generation biologics, emerging RNA therapeutics and other novel drug discovery platforms is underpinned by some key benefits.

More targeted therapies: By precisely targeting a disease's source, next-generation drugs hold promise for more effective therapies for a variety of cancers, cardiovascular diseases, inflammation diseases, metabolic diseases and even genetic diseases. Targeting can also result in safer therapies, resulting in fewer adverse events, limiting black box warnings and drug recalls which can hinder drug profitability.

New biologic targets: Next-generation therapies have opened access to diseases once thought "undruggable," including ultra-rare, often genetic, life-threatening or fatal diseases such as atypical hemolytic uremic syndrome (a rare disease causing blood clot formations and leading to stroke, heart attack, kidney failure and/or death) and spinal muscular atrophy.

Rational designs yielding longer asset duration: Drug patents most often expire at 17 years with 7 to 8 years lost to testing on average prior to marketing approval. The process gets longer as researchers contend with unanticipated adverse events.

On the front end, rational designs can lead to more predictable and exceptionally positive outcomes in trials, condensing approval time-frames and allowing companies to get their drugs to market faster—giving them more time to exclusively market. Also speeding time to market—drugs targeted for rare, life-threatening diseases and not vast populations may be granted even shorter approval timelines by the FDA.

On the back-end, unlike more traditional drugs, biologics and RNAi drugs are harder to copy, so firms can have a bigger profit potential for longer. The patent cliff becomes more of a patent slope.

While access to biologic drug technologies such as monoclonal antibodies has broadened in recent decades as the technology has matured, there still remain a limited number of thought-leading companies able to discover, develop and manufacture next-generation antibody drugs. Over the past 10 to 15 years, our team has invested in a number of these platform companies, several of which have been acquired by larger pharmaceutical companies. In less-mature fields, such as RNA therapeutics, intellectual property remains quite concentrated in early pioneering companies.

The Rise of Personalized Medicine

Advances in human biology have collided with advances in next-generation therapies to give rise to the concept of personalized medicine.

To better understand personalized medicine, consider traditional chemotherapy. Patients are given a drug or a cocktail of drugs toxic to cancer cells, but healthy cells are often collateral damage. Further, cancer drugs have variable success rates—some patients respond well to certain drugs and others not at all. Physicians have traditionally not had reliable diagnostic tools to know ahead of time who will respond and who will not.

Which means, even when successful, chemotherapy can be lengthy and painful with debilitating side effects like nausea, fatigue, sores and immunosuppression, causing an increased risk of infection. Even after a patient is cancer free or in remission, they may suffer organ damage caused by chemotherapy and radiation treatments.

But researchers increasingly understand that natural, small genetic variations can make certain therapies more effective in some people and less so or not effective at all in others. Improved diagnostic tools are being developed that can rapidly profile patient cells to help physicians determine which therapy will be most effective.

Combine that with more effective therapies that can induce a powerful, natural immune response, and/or inhibit production of the enzyme that is turning on the cancer cells and/or can deliver cell-killing toxins directly to the cancerous cells and nowhere else, minimizing side effects and cellular damage—and the promise of next-generation diagnostics and therapies is potentially massive.

The concept of personalized medicine has applications far beyond cancer and, in our view, will be an important factor in future biopharmaceutical and diagnostic innovations.

Advances in Medical Devices

Another area in which innovation has been rapid is medical devices—in diverse areas and in ways that are changing the lives of patients. For example, progress in diabetes management has made rapid advances

in recent years. Self monitoring of diabetes was first introduced several decades ago, allowing patients increased freedom and improved health. However, these systems required regular finger sticks, testing strips and portable meters in order to measure patients' blood-sugar levels. Over time, the amount of blood required for an accurate reading has declined, as has the time until the reading is rendered.

More recently, technological improvements have eliminated the need for a finger stick at all. Patients can now continuously monitor their blood-sugar levels, rather than having to remember to perform regular tests throughout the day. These developments are revolutionary for diabetes patients, and as the technology improves and becomes more affordable and accessible, it likely proves a game-changing therapy for those who live with the chronic disease.

Similarly, developments in the spinal cord stimulation market have advanced quickly recently, with the FDA approving a medical device that effectively treats patients with chronic back and leg pain. The potential market for such devices is sizeable—both in the US and globally—and there is the potential such devices may have applications in additional indications in the future. The same is largely true of the cardiovascular and other markets, where devices are increasingly technologically advanced and are shrinking in size, which makes surgery a less invasive alternative for patients who need such devices.

How Investors Can Benefit

Recent biotechnology and medical devices developments are exciting with tremendous promise. However, health care-industry research and development is still incredibly risky, and some platforms are still in very early stages. Failure rates and the cost to find out are both high—in terms of capital and time.

Further, the investable pool of innovative health care firms is large. Many of these companies do not yet have a marketed product and face binary events—approval for a first or perhaps only major pipeline drug or medical device. Approved drugs and devices can be economic windfalls, but the reverse is also true. Many health care investors aim to mitigate binary-event risk by holding a basket of relevant firms. That does diversify risk; however, our investment process is about getting large amounts of capital behind high-quality accelerating profit cycles.

To do that, we follow a highly selective process. We look for a "de-risked" profit driver—firms with one or two drugs or devices that are currently on the market or an investigational drug or device that has shown compelling clinical trial results, giving us confidence it will be approved by the FDA. Behind current profit drivers, we look for a diversified research and development (R&D) pipeline with a strong management team that has proven itself able to make good decisions about R&D investments historically. We believe we have found a few such firms across the four portfolios we manage.

The following stocks are sample holdings in each of the four portfolios Artisan Partners Growth Team manages, highlighting investment opportunities the team believes should benefit from the secular trend of health care innovation.			ARTRX	APFDX	ARTMX	ARTSX
Holding	***Profit Cycle Driver***	***In Development***				
Edwards Lifesciences	The leader in transcatheter aortic valve replacements (TAVR), one of the fastest-growing, large medical device markets globally.	In addition to its TAVR market opportunity, Edwards is assembling an interesting and early stage pipeline of novel products to treat mitral valve disease, which represents an even larger potential opportunity than the TAVR market.			•	
Genmab	Platform expertise and considerable intellectual property in the area of monoclonal antibodies, with one approved drug for lymphoma and Darzalex™ for multiple myeloma.	Beyond these successful drugs, Genmab's pipeline continues broadening thanks to early stage research partnerships with J&J, Novartis and others that are providing funding for multiple new product opportunities in coming years.	•	•	•	
Boston Scientific	A diversified developer and manufacturer of minimally invasive medical devices, including its Watchman™ atrial fibrillation device and its Lotus™ heart valve.	An impressive pipeline with devices in development in the company's areas of focus, including endoscopy, urology, cardiology and structural heart, among others.	•	•	•	
Neurocrine Biosciences	A biotechnology company focused on central nervous system and endocrine system disorders. Its drug Ingrezza™ is FDA-approved for tardive dyskinesia without requiring a black-box label regarding the possibility for suicidal side effects, which has contributed to faster uptake.	The company has promising drugs in the pipeline for other neurological disorders, including Tourette syndrome and Parkinson's disease. In addition to its recently approved Orilissa™ for endometriosis (in partnership with AbbVie), Neurocrine Biosciences has several other endocrinology drugs in various stages of development.			•	•

Investment Process Highlights

We seek to invest in companies with franchise characteristics that are benefiting from an accelerating profit cycle and are trading at a discount to private market value.

Security Selection

We seek to identify companies with franchise characteristics that are selling at attractive valuations and are benefiting from an accelerating profit cycle. We look for companies that are well positioned for long-term growth, driven by demand for their products and services, at an early enough stage in their profit cycle to benefit from the increased cash flows produced by the emerging profit cycle.

Capital Allocation

Based on our fundamental analysis of a company's profit cycle, we divide the portfolio into three parts. Garden℠ investments are small positions in the early part of their profit cycle that will warrant a more sizeable allocation once their profit cycle accelerates. Crop℠ investments are positions that are being increased to a full weight because they are moving through the strongest part of their profit cycle. Harvest℠ investments are positions that are being reduced as they near our estimate of full valuation or their profit cycle begins to decelerate. We believe that adhering to this process increases the likelihood of delivering upside participation with downside protection.

Broad Knowledge

We overlay security selection and capital allocation with the capability to invest opportunistically across the entire global equity spectrum. It is our goal to have broad knowledge of the global economy to ensure that we are able to find growth wherever it occurs. This capability extends from the design of our team, which leverages the broad experience of the portfolio managers and the deep expertise of the analysts on the team.

Team Overview

We believe deep industry expertise, broad investment knowledge, a highly collaborative decision-making process and individual accountability are a powerful combination. Since the inception of the team in 1997, we have been committed to building a team of growth investors that retains these attributes and is solely dedicated to our process and approach.

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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.

International investments involve special risks, including currency fluctuation, lower liquidity, different accounting methods and economic and political systems, and higher transaction costs. These risks typically are greater in emerging markets. Securities of small- and medium-sized companies tend to have a shorter history of operations, be more volatile and less liquid and may have underperfomed securities of large companies during some periods. Growth securities may underperform other asset types during a given period.

The views and opinions expressed are based on current market conditions as of 30 Sep 2018, which will fluctuate and those views are subject to change without notice. While the information contained herein is believed to be reliable, there is no guarantee to the accuracy or completeness of any statement in the discussion. This material is for informational purposes only and should not be considered as investment advice or a recommendation of any investment service, product or individual security. Any forecasts contained herein are for illustrative purposes only and are not to be relied upon as advice or interpreted as a recommendation.

For the purpose of determining the Funds' holdings, securities of the same issuer are aggregated to determine the weight in the Fund. Securities named in the Commentary; but not listed here are not held in the Fund(s) as of the date of this report. The holdings mentioned above comprise the following percentages of the Funds' total net assets as of 30 Sep 2018: Artisan Global Opportunities Fund — Boston Scientific Corp 3.3%, Genmab A/S 2.1%. Artisan Global Discovery Fund — Boston Scientific Corp 3.3%, Genmab A/S 1.5%. Artisan Mid Cap Fund — Boston Scientific Corp 3.2%, Edwards Lifesciences 2.4%, Genmab A/S 1.3%, Neurocrine Biosciences Inc 1.3%. Artisan Small Cap Fund — Neurocrine Biosciences Inc 1.9%. Portfolio holdings are subject to change without notice and are not intended as recommendations of individual securities. Securities named in the commentary but not listed here are not held in the Fund as of the date of this report.

Our capital allocation process is designed to build position size according to our conviction. Portfolio holdings develop through three stages: Garden℠, Crop℠ and Harvest℠. Garden℠ investments are situations where we believe we are right, but there is not clear evidence that the profit cycle has taken hold, so positions are small. Crop℠ investments are holdings where we have gained conviction in the company's profit cycle, so positions are larger. Harvest℠ investments are holdings that have exceeded our estimate of intrinsic value or holdings where there is a deceleration in the company's profit cycle. Harvest℠ investments are generally being reduced or sold from the portfolios. **Private Market Value** is an estimate of the value of a company if divisions were each independent and established their own market stock prices.

This material is provided for informational purposes without regard to your particular investment needs. This material shall not be construed as investment or tax advice on which you may rely for your investment decisions. Investors should consult their financial and tax adviser before making investments in order to determine the appropriateness of any investment product discussed herein. We expressly confirm that neither Artisan Partners nor its affiliates have made or are making an investment recommendation, or have provided or are providing investment advice of any kind whatsoever (whether impartial or otherwise), in connection with any decision to hire Artisan Partners as an investment adviser, invest in or remain invested in any funds to which we serve as investment adviser or otherwise engage with Artisan Partners in a business relationship.

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