The health care breakthrough that's not an obesity drug

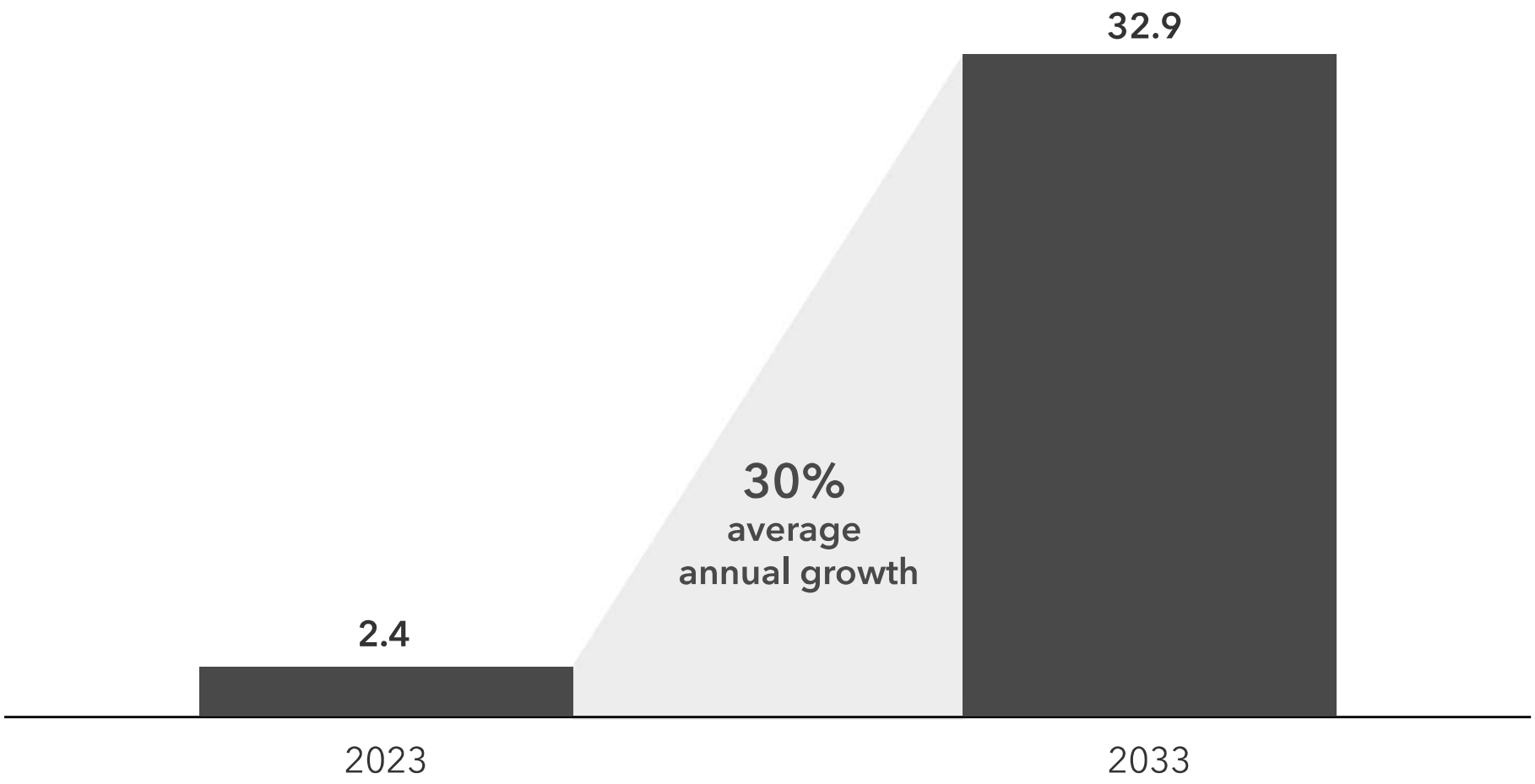
You've heard of computer hacking, now meet gene hacking. In an age of remarkable health care innovation, scientists are manipulating human DNA to find new ways to treat diseases.

They've moved from the lab to the real world with a treatment for the life-shortening disease sickle cell – the first approval based on a revolutionary gene-editing technology known as CRISPR.

"Whether it's biotechnology or medical devices, there has always been an important moment that has changed how investors view a new technology or therapy. It could be one major success or a series of successes, and we are seeing pockets of that now across health care," says Rich Wolf, portfolio manager for The New Economy Fund®.

Gene editing is set to expand over the next decade

Estimated global market size of CRISPR gene editing (USD billions)



Source: Statista. As of January 2023. CRISPR stands for "clustered regularly interspaced short palindromic repeats."

Novo Nordisk's and Eli Lilly's weight loss drugs, originally developed for the treatment of diabetes, are prime examples. The drugs, sold under the brand names Ozempic, Wegovy and Zepbound, could reshape industries beyond health care.

Meanwhile, cell and gene therapy companies are forging their own paths. These therapies can modify, replace, activate and disable genes. And rather than outright change human DNA, some companies are working on ways to moderate or fine-tune how they're expressed.

"Approvals for genetic disorders based on a single gene such as sickle cell are just the beginning for gene-editing therapies," Wolf says. "There will be more to come, but it won't be a linear progression. We need to see these technologies work for diseases that affect a wider patient population. There's a lot of wood to chop before that happens, but I believe we will get there."

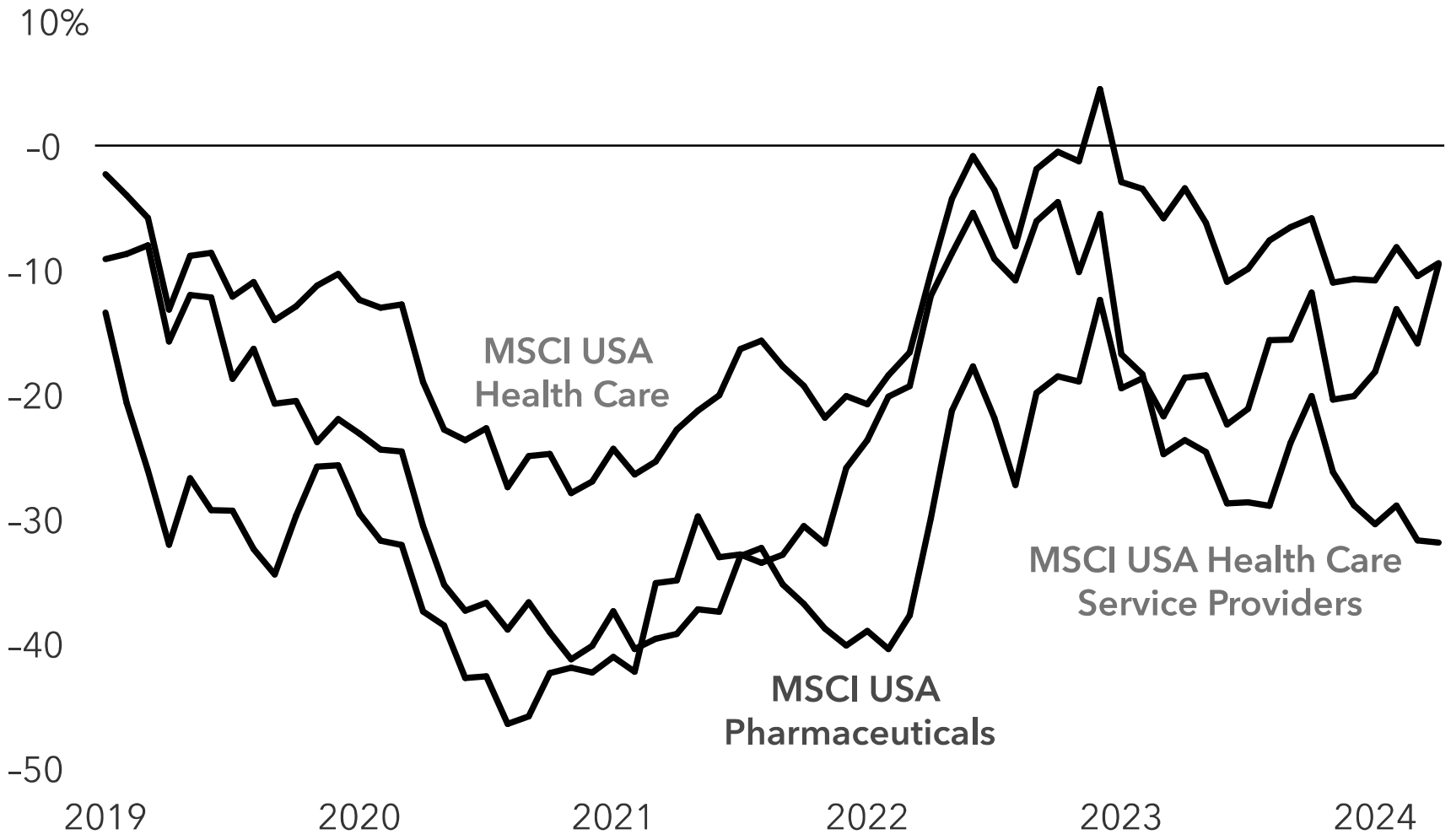
The science and the share price

Biotech investing is notorious for hype not quite meeting reality. More recently, the Federal Reserve's monetary tightening policy siphoned capital away from more speculative investments like biotech.

Many companies were also caught flat-footed as demand for pandemic-era innovations, such as vaccines, dropped faster than projected, adds Wolf. "There was tremendous excitement over anything that was going to treat the pandemic, and valuations spiked in a big way. The bubble has since burst, particularly for companies with their revenue potential tied to the pandemic."

Health care stocks appear undervalued relative to the broad market

Relative P/E valuations — MSCI USA Health Care and sub-sectors vs. MSCI USA



Sources: Capital Group, MSCI. Relative valuation is the ratio between the forward 12-month price-to-earnings (P/E) ratio of the health care-related sectors and the MSCI USA Index. P/E for a stock is computed by dividing the price of a stock by the company's annual earnings per share. A value below zero indicates that health care is relatively undervalued. As of April 24, 2024.

Nevertheless, it's an industry that long-term investors can't ignore. Health care spending in the United States reached $4.5 trillion in 2022, according to the Centers for Medicare and Medicaid Services, or 17.3% of U.S. GDP. Valuations have improved for industries within health care. Since the start of 2024, investors have returned to health care stocks. And if interest rates decline, that could support continued capital flows into the industry.

When you're on the cutting edge of science, there will always be failures. Significant hurdles remain for widespread adoption of cell and gene therapies, and health care investing is a decades-long endeavor. "The framework I follow considers the potential future earnings and the probability of success. In the case of biotech, I like to start with small allocations, which I'll add to once the technology passes the threshold of helping a larger patient population or disease," Wolf explains.

Biotech charges forward

Health care companies are racing to define how diseases are treated. Cell and gene therapy companies — including Vertex Pharmaceuticals, Gilead Sciences and Amgen — are going after the same diseases that weight loss drugs are targeting in the kidney, liver and heart, as well as cancers, autoimmune disorders and others.

Companies are developing cell and gene therapies for many diseases

Largest pharma and biotech companies with gene and cell therapies in development

Company	Headquarter and market capitalization	Target diseases
AstraZeneca	United Kingdom **$233B**	Rare diseases, metabolic disorders
Novartis	Switzerland **$224B**	Rare genetic diseases
Roche	Switzerland **$168B**	Hemophilia, Huntington's, spinal muscle atrophy, ophthalmology
Amgen	United States **$144B**	Oncology and rare diseases
Pfizer	United States **$143B**	Single-gene defects, neuromuscular and hematologic diseases
Vertex	United States **$102B**	Cystic fibrosis, sickle cell disease, beta thalassemia

Sources: Capital Group, MSCI, Drug Discovery & Development. Company examples include constituents of the MSCI All Country World Pharmaceuticals, Biotech and Life Sciences Index that fall within the top 15 largest companies by market capitalization and have gene editing

and cell engineering candidates in current development as of March 10, 2023. Market capitalizations as of April 25, 2024.

In the case of cell therapy, cells are modified outside the body and then infused into patients. One specific type is commonly known as CAR-T. It has gained approval to treat certain blood cancers. CAR-T stands for chimeric antigen receptor, with the T referring to a type of immune cell modified to find and destroy cancer cells.

Current CAR-T treatments use a patient's own cells and are limited by the long, complex journey involved for patients, manufacturing challenges and high costs. "Treatments may become more accessible and safer as scientists develop off-the-shelf techniques derived from unrelated donor cells," says biopharmaceuticals and biotechnology analyst Christopher Lee. "Additionally, I believe companies will go beyond using T-cells and incorporate other types of cells over the next decade."

Another area of cell engineering is focused on modifying stem cells to replace missing or defective cells. For example, Vertex aims to cure Type-1 diabetes by transplanting insulin-producing cells into the pancreas, a program currently in human clinical trials.

Yet another promising innovation is RNA-interference (RNAi). This technology allows companies to create highly specific therapies that turn off the production of proteins that cause disease. Biotech company Alnylam is currently developing programs in areas such as heart failure, hypertension and Alzheimer's.

"The idea that you're not irreversibly changing the DNA is compelling, but like most health care innovation, safety is paramount," says equity analyst Judith Finegold, who focuses on U.S.-based biopharmaceuticals.

Every patient population has a different risk profile. "There are programs underway to irreversibly gene edit your liver to treat high cholesterol, and in 15 years that could be the answer, but we need to really understand the safety profiles for drugs because having high cholesterol is not a death sentence," she adds.

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