CREATING CURES, SAVING LIVES:

The Urgency of Strengthening U.S. Pharmaceutical Manufacturing

NATIONAL ASSOCIATION OF Manufacturers

The pharmaceutical industry plays a vital role in the United States economy, yielding substantial contributions in terms of job creation, labor income, value-added output, and overall economic contribution. Companies within this sector range from large multinational corporations that develop and distribute a broad spectrum of prescription drugs to firms specializing in biopharmaceuticals, generic medications, and over-the-counter products. Additionally, there are businesses focused on producing active pharmaceutical ingredients, creating vaccines, and manufacturing medical biologics.

The industry plays a pivotal role in the nation's economy, supporting jobs for nearly 1.5 million people. That is larger than the entire workforce in 18 out of the 50 U.S. states. These employment opportunities translate to a remarkable $147 billion in labor income, emphasizing the industry's profound influence on the livelihoods of countless families. Furthermore, the industry generates an impressive $147 billion in labor income, indicating its significant economic impact on workers and their families. The sector's total value-added output, or its gross output minus its cost of intermediate inputs like raw materials, is a substantial $355 billion, reflecting its strong contribution to the value created within the economy. Pharmaceutical and medicine manufacturing industry activity generates a remarkable $655 billion in economic output each year, underscoring its substantial influence on the overall economic performance of the nation.

Research and development (R&D) investments serve as the lifeblood of the pharmaceutical and medicine manufacturing industry, driving innovation, breakthrough discoveries, and the development of new drugs and therapies. These advancements directly contribute to the enhancement of patient care and the reduction of mortality rates. By constantly pushing the boundaries of medical science, countless lives are saved and improved every year.

Strengthening the resilience of this industry requires a continued commitment to R&D, ensuring a sustainable pipeline of new treatments, improved healthcare outcomes, and advancements in medical science. By fostering a supportive environment for R&D with elements like strong IP protection, effective technology transfer policies, and positive incentives to invest, policymakers and stakeholders can enhance the industry's ability to respond to emerging public health challenges, adapt to evolving healthcare needs, and maintain its position as a global leader in pharmaceutical innovation. The industry invests in an uncertain future, but this investment requires a regulatory environment that is certain and supports innovation.

Executive Summary

This report presents an analysis of the direct impact of the pharmaceutical manufacturing industry on the overall economy, focusing on factors like output and labor income. Additionally, it offers a comprehensive assessment of the industry's economic contributions by examining its influence on other sectors in the United States, including the industry's broader influence and impact on Americans themselves.

The pharmaceutical manufacturing industry is a vital contributor to the U.S. economy. The industry also generates economic activity in other sectors when it purchases services and goods as inputs for the development and production of its products. The economic impacts created within these supply chains are known as indirect effects. Moreover, employees working in the pharmaceutical manufacturing sector and its associated supply chains spend their earnings in downstream sectors, resulting in a range of economic activities at local and national levels. These contributions are referred to as induced effects. The overall economic impact of the pharmaceutical and medicine manufacturing sector encompasses these direct, indirect, and induced effects.

FINDINGS:

The pharmaceutical manufacturing industry is a major contributor to the U.S. economy, and its impact is growing.

- The industry accounted for $355 billion in value-added output to the U.S. economy in 2021. The direct contribution from the industry of $192 billion is up 24% from just 2 years ago. The pharmaceutical sector was already an economically vital sector before the pandemic, and it has become increasingly more important in its aftermath.
- Pharmaceutical and medicine manufacturing generates a total of $655.2 billion in annual output. Each dollar generated by the pharmaceutical and medicine manufacturing sector generates an additional $0.85 in output elsewhere in the economy.

The pharmaceutical manufacturing industry fuels other sectors of the economy, supporting nearly 1.5 million jobs in America.

- The industry directly employs an estimated 291,000 workers in the United States, an increase of nearly 9% in the last 24 months.
- One job in the pharmaceutical manufacturing industry helps support 4.1 other jobs in the overall workforce. Add these jobs to the jobs in the pharmaceutical manufacturing sector, and the industry supports one in every 20 jobs in the U.S. economy.

Industry employees are highly productive.

- Industry employees produce $1.2 million in output per employee. This is nearly six times more than the U.S. economy's average output per employee ($208,084).

A successful pharmaceutical ecosystem requires strong private-sector investment.

- In 2021, pharmaceutical companies invested more than $102 billion in R&D. A recent study from the National Science Foundation's National Center for Science and Engineering Statistics estimates that the pharmaceutical and medicine manufacturing sector alone accounts for 17.1% of total R&D investment in the United States.
- The pharmaceutical industry invests 16.6% of its sales back into R&D. Indeed, the U.S. pharmaceutical industry invests nearly 3.5 times more in R&D as a percentage of sales than the average U.S. industry.

The pharmaceutical manufacturing industry pays high wages and benefits to American workers.

- Annual average labor income per worker in the pharmaceutical manufacturing industry is more than $184,000. This figure is higher than some of the highest-paying industries in the country, including finance and insurance ($100,000), professional, scientific and technical services ($109,000, and management ($146,000), and roughly 2.5 times the U.S. workforce average income ($73,000).

The industry creates valuable STEM jobs.

- While roughly 6.6% of the U.S. workforce has a STEM occupation, some 25% of all jobs in pharmaceutical and medicine manufacturing are STEM-related. The pharmaceutical manufacturing sector employs more than four times the percentage of STEM workers employed in the overall workforce.

Price control policies, like those in the Inflation Reduction Act (IRA), may hurt U.S. pharmaceutical leadership.

- Price-control legislation, like the IRA, may negatively impact the industry's R&D efforts, investment landscape, and overall economic contributions.
- Price controls may deter advancements in healthcare and negatively impact the nation's economic prosperity.
- The IRA was designed to impose drug price controls and may have unexpected consequences.

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Introduction

The decline in cancer-related deaths serves as a compelling case study for the importance of a strong biopharmaceutical sector, the innovation it creates, and the positive outcomes this innovation achieves. In 2020, the mortality rate associated with cancer declined by an estimated 1.5%. This was not a one-time decline influenced by exogenous environmental factors, but part of a broad trend that has culminated in a 33% reduction in cancer-related deaths in the United States since 1991.[1] This decline translates into nearly 4 million fewer deaths over the last 30 years.

The decline in cancer-related deaths has been especially pronounced over the last 5 years. For example, mortality rates for leukemia, melanoma, and kidney cancer have each declined approximately 2% annually over this time period despite stable or even increasing incidence rates for these diseases. This decline in cancer-related mortality rates reflects increased early detection, advancements in treatment, and the development of targeted therapies.

As impressive as these developments are, the success of these new drugs are the result of pharmaceutical innovation within an ecosystem that ensures R&D costs can be recouped and future R&D expenditures can be funded. At its core, the US pharmaceutical industry is sustained by the symbiotic relationship between revenue, R&D, and strong IP protection. Revenue acts as the lifeblood of the industry, enabling pharmaceutical companies to finance critical R&D efforts. These research endeavors are fundamental to the discovery and development of innovative drugs and treatments that can significantly improve human health and save lives.

Robust IP protection plays a vital role in incentivizing and safeguarding these substantial investments in R&D. It grants pharmaceutical manufacturers sufficient time to recoup costs that are poured back into research and thereby close the circle of medicine innovation. The close alignment between revenue, R&D, and IP protection forms a dynamic ecosystem that drives the ongoing progress and growth of the U.S. pharmaceutical industry, leading to breakthrough advancements and the improvement of global healthcare.

Cancer deaths will likely only continue to decline within an ecosystem that has strong R&D and robust IP protections. As we look ahead to the future, sustaining the progress made in reducing cancer-related mortality requires continued investment. The pharmaceutical industry's ability to innovate and develop cutting-edge therapies relies on a stable revenue stream, which, in turn, depends on strong IP protection. This symbiotic relationship is fundamental to fostering an environment where groundbreaking discoveries can thrive.

Innovation in the pharmaceutical sector is a complex and expensive process. It often takes years of research, clinical trials, and regulatory approval before a new drug can be brought to market. The protection of intellectual property through patents grants pharmaceutical manufacturers the exclusive rights to their discoveries for a limited period, allowing them to recoup the substantial costs associated with R&D.

Without robust IP protections, the incentives for companies to invest in the risky and resource-intensive process of drug development would diminish significantly. This could result in a slowdown of progress and the potential loss of many promising therapies that could have otherwise improved patients' lives.

The decline in cancer-related deaths over the last three decades demonstrates the remarkable impact of pharmaceutical innovation within a supportive ecosystem. The close interplay between revenue, R&D, and IP protection has been instrumental in driving progress and advancements in the U.S. pharmaceutical industry, ultimately leading to significant improvements in global healthcare. By maintaining this dynamic ecosystem, we can continue

to build on the progress made and strive towards a future with even fewer cancer-related deaths, providing hope and better health outcomes for millions of people worldwide.

While there have been significant strides in areas such as cancer treatment, there remain disease states that have yet to see major outcome improvements. Conditions like Alzheimer's and Parkinson's continue to be formidable challenges. Despite extensive research and investment, effective treatments for many ailments remain elusive. It's a stark reminder that, as much as we've achieved, there is still a considerable journey ahead. The financial health of the pharmaceutical industry, buttressed by robust IP protection and sustained R&D investments, is paramount in the quest to push the boundaries of medicine and improve global health outcomes.

This paper showcases the possibilities that emerge when the pharmaceutical industry is provided with a fertile environment for investment and growth. Beyond the realm of improved health outcomes, the pharmaceutical sector also serves as a substantial contributor to the U.S. economy. The pharmaceutical manufacturing industry plays a pivotal role in bolstering economic activity not only within its own sector but also in various industries through its procurement of goods and services necessary for drug development and production. These ripple effects, known as indirect impacts, generate additional economic benefits throughout the broader economy.

Moreover, the workforce employed in the pharmaceutical manufacturing sector and its associated supply chains significantly contributes to the economy. Their spending habits in downstream sectors initiate a chain of economic activities, fostering growth and stability at both local and national levels. These contributions, referred to as induced effects, hold immense potential for shaping economic progress.

This paper sheds light on cautionary tales arising when investment in the pharmaceutical sector is stymied by the detrimental impacts of price-control policies, such as those included in the Inflation Reduction Act (IRA). It also highlights risks that the IRA may hinder efforts to combat chronic conditions such as President Biden's Cancer Moonshot. By understanding the critical role of a conducive ecosystem, we can work towards sustaining and strengthening the industry's positive impact on global healthcare and the U.S. economy.

Funding Future Cures and Ensuring Pharmaceutical Manufacturing Thrives

Pharmaceutical manufacturers invest heavily in R&D in order to continue developing new treatments and therapies. The industry invests 20 times more than it did in the 1980s. In fact, over the last 40 years, pharmaceutical R&D investment has compounded at over 9% a year. Today, the industry invests over $100 billion annually to create new medicines.[2]

The industry is investing at a historic pace because the cost to bring new medicines to market is astronomically high. The average cost of developing a new drug was $2.3 billion in 2022, increasing $298 million from the prior year.[3] Ever-rising costs are driven by numerous factors. It can take 10 to 15 years to create an effective medicine and bring it to market. Along the way, drug candidate failure rates exceed 90%, and even 90% of those that advance to phase I clinical trials fail.[4] In all of this, pharmaceutical manufacturers are increasingly tackling some of the most difficult of diseases like Alzheimer's, amyotrophic lateral sclerosis (ALS), Parkinson's, and rare genetic disorders.

The pharmaceutical industry is one of the most R&D-intensive industries in the country. The National Center for Science and Engineering Statistics (NCSES) estimates the pharmaceutical and medicine manufacturing sector alone accounts for roughly 17.1% of total R&D investment in the United States. Put another way, R&D investment in the United States would be nearly a fifth smaller if not for the pharmaceutical industry.

Despite significant industry investment, a return on this investment is far from guaranteed. In fact, the estimated returns on investment (ROI) in pharmaceutical R&D have fallen to just 1.2%, the lowest ROI observed in the last 13 years.[5] Record levels of R&D investment will be required in the years ahead in order to continue the success the industry has achieved in the past two decades of lowering mortality rates and improving quality of care rates, all of which have been achieved through new innovative medicines and treatments.

The foundation for R&D investment in the pharmaceutical industry starts with sales, and the pharmaceutical industry allocates a substantial portion of its sales to future drug discovery. NCSES estimates nonmanufacturing industries invest roughly 4.1% of their sales into R&D, but the pharmaceutical industry invests 16.6% of its sales back into R&D.[6] Indeed, the U.S. pharmaceutical industry invests on average more than three and half times more in R&D as a percentage of sales than the average U.S. industry.

While government investment in life sciences is important, the discovery of new medicines and treatments are being driven by private investment. Chakravarthy et al. find private-sector R&D accounts for 73% of major milestones in drug development phases and 81% in the manufacturing phase over the past 25 years.[7] Between 2010 and 2019, the number of new drugs approved for sale increased 60% compared with the previous decade.[8] These new life-saving and life-enhancing drugs are a direct result of private investment in drug R&D made by the pharmaceutical industry.

The pharmaceutical industry is also taking on an increasingly important role in funding and conducting basic research, to the benefit of multiple industries. Businesses funded an estimated 35% of all U.S. basic research in 2021, up from less than 17% in 2000. The doubling in the share of basic research being funded by businesses in the United States is largely the result of substantial expansions in basic research undertaken by the pharmaceuticals and medicines industries. Over the same period, the federally funded share declined from roughly 58% in 2000 to an estimated 40% in 2021.[9]

Pharmaceutical R&D investment does more than fuel new medicine development. It also ensures a robust pipeline for low-priced generic drugs, all of which are the result of prior R&D investment. Any policy interventions that curtail or reduce revenue inevitably lead to diminished future investments. Consequently, reductions in the development of innovative medicines will impede the advancement of generic alternatives.

Furthermore, the positive effects of R&D extend beyond the immediate outcomes. R&D investment serves as a crucial catalyst for future economic growth. R&D plays a pivotal role in driving total factor productivity and increasing output per employee. Firms and industries do not have the ability to fully capture the comprehensive benefits derived from their R&D expenditures. In other words, the advantages of a company's R&D spending extend not only to that specific entity but also to a broader spectrum of firms within the economy. Economic estimations indicate a 1% increase in total R&D results in a 0.06% to 0.61% rise in economic output. In simpler terms, this means that when businesses invest in R&D, the whole economy can benefit. Essentially, private R&D investment extends far beyond the company making the investment and can lead to bigger gains for the broader economy. [10]

The R&D intensity of the pharmaceutical industry is also evident in its workforce. Roughly 8.5% of domestic U.S. business employment is R&D jobs. For overall manufacturing, the share is approximately 9.5%, but in the pharmaceutical industry, some 21.5% of the industry workforce is focused on R&D.

A global analysis further highlights the importance of U.S. pharmaceutical industry R&D. Manufacturing is the primary focus of business R&D investment in most top R&D-performing countries. The manufacturing sector accounted for more than half of the total business R&D in the United States (62%). Germany (85%), China (91%), Japan (87%), and South Korea (89%) each had even higher manufacturing shares of business R&D compared to the United States. While pharmaceutical industries in other countries invest in R&D, the intensity of R&D investment in the United States is significantly unique. No other country is close to the United States when it comes to the total share of business R&D attributed to the pharmaceutical manufacturing sector as Table 1 illustrates.

The significant level of investment is a result of robust government policies that effectively promote and support R&D investments. These policies guarantee the protection of investments in groundbreaking products and provide opportunities for recovering costs through future sales. Companies determine their R&D investment by considering the projected revenue from new products, estimated expenses for their creation, and various factors influencing the supply and demand of drugs. Modifying these policies will diminish investment in therapies that save lives.

TABLE 1. R&D BUSINESS EXPENDITURES BY COUNTRY

Millions of U.S. PPP* Dollars and Percent of Total Business Enterprise

	United States (2018)	France (2017)	Germany (2018)	United Kingdom (2018)	China (2018)	Japan (2018)	South Korea (2018)
Pharmaceuticals, medicinal chemical, and botanical products	$74,592	$1,079	$7,094	$658	$13,741	$13,545	$1,825
	16.9%	2.5%	7.2%	1.8%	3.8%	9.9%	2.3%

*Purchasing Power Parity

A Conversation with RHONA O'LEARY

Senior Vice President, PD Portfolio Strategy & Execution, GENENTECH

What is the impact of pharmaceutical price controls, like those in the Inflation Reduction Act, on the broader pharmaceutical industry?

Price controls like those in the IRA are introduced with the stated intent of making medication more affordable and accessible to patients, but in reality, often have unintended consequences on drug development. Price controls can stifle innovation, significantly complicate decision-making within pharmaceutical companies in terms of the therapies they choose to pursue, and ultimately prevent patients from getting access to the best medications at the earliest possible time.

We can see some of these unintended consequences of price setting and price controls in the EU market, which have resulted in delayed market entry, drug shortages, parallel trade, reduced innovation, and a shift of R&D towards the United States.

Generally speaking, a pharmaceutical company such as Roche puts patient needs at the forefront of decision-making, but also needs to consider various business aspects in order to remain viable. These include R&D decisions, business model considerations, and decisions on which drugs are researched and brought to the market.

The average cost to bring a new drug to market is $2.5 billion. A significant portion of the price of a drug is intended to recoup these costs and fund research. Roche spends $15 billion a year on R&D. Price controls can significantly reduce the potential returns on investment for new drugs leading to companies being more risk averse in their R&D and resulting in decreased innovation.

Companies are faced with a number of business model considerations. They could choose to pivot to disease areas where the potential market is larger or where they can develop blockbuster drugs that may treat common ailments at the cost of rare diseases or conditions that are much harder to treat or require significant investment. For example, Roche has invested billions in Alzheimer's R&D with no drug on the market yet.

Price controls can also affect where companies choose to first launch new medicines. If companies are unable to achieve their desired return on investment in one country due to price controls, they might prioritize launching products in other more lucrative markets first.

What areas of the industry will be most severely impacted by the IRA's provisions on drug pricing?

The greatest impact will be in terms of investment choices companies make. We are watching a number of areas: how manufacturers prioritize or deprioritize certain types of molecules or therapeutic areas; how capital flows to smaller startups and how deals focusing on the riskiest disease areas change; and how commercialization strategies change.

There may be incentive for manufacturers to focus on younger populations thereby compromising the healthcare needs of older patients. We might see lower investment in highly convenient small molecule drugs which are usually administered orally, allowing patients to take them on their own, in favor of large molecule drugs administered by health care professionals through IV or other means. And we might see fewer new therapies developed using innovation from existing products. All of these ultimately challenge the ability of the U.S. pharmaceutical sector to remain at the forefront of drug development and innovation.

How will price controls impact R&D?

Price controls will have an impact on the entire drug development life cycle from research and development through commercialization. From a pipeline R&D perspective, there could be an impact on what types of drugs companies pursue, potentially limiting therapies for diseases with smaller patient populations. Companies may also need to make investment decisions based on whether competitors' drugs in a given disease area would be up for negotiation.

From a new investment perspective, companies may decrease investment in highly convenient small molecules in favor of large molecules, which must be administered by a healthcare professional. It is important to note that there are other charges and markups associated with medication being delivered in a clinical setting, such as hospitals charging two times to five times the list price.

These types of regulations create an incentive to consider what disease areas to target beyond purely scientific or patient benefit rationale. For example, companies might consider delaying the development of treatments for diseases with smaller patient populations until a more commercially attractive drug can be launched.

Which pipeline projects are likely to be most negatively impacted and why does that matter?

While it is too early to say how this will play out in the short term, we can certainly expect to see an impact across several therapeutic areas such as oncology, rare disease, and immunology. Our drugs in those areas, such as Rituxan, Xolair, Actemra, and others, took a great deal of time and investment from R&D to commercialization – which we would have been unlikely to pursue if they were launched in the current era.

We are also less likely to enter a new therapeutic area where we might expect to have one or more negotiated products potentially subject to "payer management" – the practice in which

insurers seek to dictate patient treatment plans. For example, cancer immunotherapies are often subject to these controls, as are treatments for diseases where there is a higher Medicare population such as ophthalmology, autoimmune, respiratory, or infectious disease), disincentivizing investment in these areas.

Consider some of the drugs we have launched in the past. Herceptin was approved in 1998 for metastatic breast cancer. This was followed by further research on the drug, which resulted in an approval for adjuvant breast cancer, providing significant additional benefits to patients. This indication was launched in 2006, several years after the original drug had been approved. If it had been a small molecule under the IRA, we would have had much more limited time to get a return on an enormous investment, likely jeopardizing that scientific advancement and patient benefit.

When would you expect to see these impacts materialize, and how are the short-term impacts different from the long-term impacts?

The short-term impact of the price controls will vary by pharmaceutical companies depending on the level of exposure they have to negotiation, along with where companies will need to adjust their strategies most aggressively on the commercial side or the R&D side. There may be different types of exposure in the short and long term. A drug may fall on the negotiated list resulting in immediate adjustment of the commercial strategy to compensate for the loss of revenue. Alternatively, a drug may be in the same class as a potentially negotiated drug, whereas a pharma company may choose a defensive play given the potential price impact within the class.

The more medium-to-long-term impact is on choices pharma companies may be forced to make to divest from certain treatment areas that may be disproportionately impacted by price controls, choosing to exit or not enter certain diseases and reducing early R&D investment in specific diseases areas or modalities.

Cautionary Tales

The United States leads the world in pharmaceutical innovation by myriad measures. It is home to seven out of the top 10 pharmaceutical companies with the highest R&D expenditures worldwide. Nearly 150,000 clinical trials have taken place in the United States since 2008. France is a distant second with roughly 30,000 trials.[11] The United States accounts for over 40% of total global pharmaceutical and biotechnology patents since 1985.

In 2022, U.S.-based pharmaceutical manufacturers exported over $80 billion in pharmaceutical products, behind only Switzerland and Germany. Notably, U.S. pharmaceutical exports have more than doubled over the last decade, far exceeding the growth in exports of other major pharmaceutical markets. In other words, U.S. pharmaceutical manufacturers are gaining a larger share of global exports. Pharmaceutical exports are important because they help pharmaceutical manufacturers scale innovative medicines, thereby recouping R&D expenditures and fueling the next round of drug discoveries.

The United States' pharmaceutical leadership is not by accident. It is the result of private R&D investment, broader investment in life-sciences research, strong IP protection, effective technology transfer policies, positive incentives to invest, and drug-pricing policies that encourage drug development. But this leadership is not guaranteed, and altering the trajectory of the domestic pharmaceutical industry by changing these foundational policies could have grave results for the overall industry, for economic growth, and for the people who rely on these life-saving therapies.

CANADA'S SLIDE

A number of countries have had strong pharmaceutical industries in the past but have lost their leadership roles due to policy changes. In Canada, for example, slow and burdensome drug-listing processes, poor intellectual property protection, and other regulatory changes have gutted the domestic pharmaceutical industry.[12] Canada was one of the slowest countries to begin COVID vaccinations, despite having the highest proportion of fully vaccinated individuals by February 2022. The disconnect was a result of Canada not having domestic capacity to produce COVID vaccines. In the United States, over 1 million COVID vaccines were being administered a day by December 23, 2020, just 10 days after the first vaccination was administered. By the end of January 2021, over 30 million COVID vaccinations were being administered each and every day in the United States. In Canada, less than 2.8 million total vaccinations had been administered by the end of January 2021, and it would not be until March 2021 that COVID vaccinations began fully accelerating.

It was not that Canada did not have enough capacity to satisfy demand; it was that they had none at all. They lost their manufacturing capability after years of neglect that saw vital pharmaceutical manufacturing resources move elsewhere. Canada was forced to import COVID vaccinations from abroad and could only begin importing direly needed vaccines after these countries had satisfied their own domestic demand. While it is difficult to know the exact economic damage caused by the delayed vaccination rollout, a study from the C.D. Howe Institute estimates a 6-month delay in vaccinations in Canada would have led to economic losses equivalent to about 12.5% of GDP, or about $156 billion in economic activity in 2021.[13] Canada has since pledged over $1.3 billion for 12 new or expanded biomanufacturing plants, but most are still in construction or bogged down by regulatory hurdles that have encumbered needed technology transfer. Canada has yet to produce COVID vaccines domestically.[14, 15]

Canada's slide began in 1969, when the Canadian government made changes to the Patent Act, allowing for compulsory licensing. This meant that generic drug manufacturers in Canada could produce

drugs that were newly patented in the United States or other countries by simply notifying the patent holder and paying a fixed royalty fee of 4%. While this policy helped reduce drug prices in Canada, it did so at the expense of Canada's domestic pharmaceutical industry, in effect making Canada dependent on the rest of the world for pharmaceuticals. The policy also had negative effects on economic output and, more importantly, domestic investment in R&D for new medicines.

In 1983, the Federal Minister of Consumer and Corporate Affairs recognized the need to stimulate growth in the pharmaceutical industry and called for a rebalancing of the 1969 policy. Subsequently, in 1987, Bill C-22 was passed, amending Canada's Patent Act and bringing significant changes to the compulsory licensing system. Over the following years, additional reforms were made as Canada modified the Patent Act and implemented agreements related to intellectual property rights under the Agreement on Trade-Related Aspects of Intellectual Property Rights and the provisions of the North American Free Trade Agreement.

As a result of these changes, there was a notable increase in R&D investment. Prior to the passage of Bill C-22, R&D spending in Canada as a percentage of sales was less than 5%. However, from 1988 to 2002, R&D spending rose from $165.7 million to $1.198 billion. By 2002, R&D investment as a percentage of sales reached 9.9%, peaking at 11.7% in 1995.

Unfortunately, these positive economic developments were short-lived. In the 2000s, the Canadian government took an aggressive approach to drug pricing. Simultaneously, the Canadian Federal Courts started invalidating entire patents based on a principle known as "The Promise Doctrine." According to this doctrine, to meet the requirements of the Patent Act, an invention's usefulness had to be demonstrated or reasonably predicted based on the patent's filing date. Failure to meet this condition resulted in the invalidation of the entire patent.

Although the Supreme Court of Canada overturned The Promise Doctrine in a landmark decision in 2017, the damage had already been done. After experiencing a growth of over 600% between 1988 and 2002, R&D investment in Canada declined by more than 25% over the following 20 years. In

2019, total R&D expenditures amounted to $893.2 million. Presently, Canada heavily relies on importing intellectual property and allocates only 3.9% of total sales to R&D, the lowest level since data have been available.

Canada's pursuit of policies that hinder domestic pharmaceutical investment persists. Most recently, the country has taken steps to lower drug prices, leading to increased market uncertainty. The Medicine Prices Review Board, a quasi-judicial agency in Canada, sets the maximum prices that pharmaceutical companies can charge for drugs within the country. Currently, the board uses a list of comparison countries to establish price thresholds, but upcoming rule changes will exclude certain jurisdictions like Switzerland and the United States. This change will result in decreased maximum allowable prices in Canada and may prevent the availability of some innovative medicines. Because pharmaceutical companies invest significant

resources in developing innovative drugs, they rely on favorable pricing conditions to recoup these investments in order to fund future R&D initiatives. When the potential returns from the Canadian market are diminished due to lower maximum allowable prices, companies might prioritize launching their products in other countries where they can achieve better economic outcomes.

Comparatively, reimbursement times in Canada, which determine how long it takes for a drug to be listed on a drug plan and made available to patients, are significantly slower than those in the United States and many OECD nations. This situation erodes patent exclusivity periods for innovative companies operating in Canada and delays Canadian patients' access to new treatments. On average, a new medicine takes over 2 years from initial Health Canada approval to the first Product Listing Agreement.[16]

Canada has created an unpredictable regulatory regime for the biopharmaceutical industry, leading pharmaceutical companies to relocate their operations elsewhere.

JAPAN'S UNFULFILLED POTENTIAL

At one point, Japan was one of the premier leaders in pharmaceutical development and manufacturing, but strong drug price controls significantly damaged the domestic industry by restricting the industry's ability to invest in new medicines.

Japan's pharmaceutical industry grew rapidly in the aftermath of World War II. By 1963, Japan had become the second largest producer of pharmaceuticals, behind only the United States.[17] By 1982, Japan invested more in pharmaceutical R&D than any other country besides the United States.[18]

Japan's strong pharmaceutical R&D investment would drive significant drug discovery. Japan-headquartered enterprises introduced 29% of the world's new chemical entities, essentially new drugs, in the 1980s, far eclipsing other

pharmaceutical powerhouses like Switzerland, which accounted for 11% of the new drugs introduced during the decade, and Germany, which introduced about half as many new drugs as Japan did during that time.

Fast forward to the most recent decade, and Japan's share of new medicine introductions has fallen from 29% to 7%.[19] Japan's burgeoning leadership in pharmaceutical innovation and domestic production was stymied by a series of well-meaning policies that disrupted a delicate ecosystem. As Japan's population aged, the Japanese government introduced a number of policies to contain costs and pharmaceutical production in Japan began to fall in the aftermath of these policies.

Certainly other factors have contributed to Japan's decline. But as Maki Umemura notes, "The biennial price reductions had a particularly severe impact on Japanese pharmaceutical firms' incentives to invest in R&D."[20] Research from Professors Heather O'Neill and Lena Crain suggests price regulation in Japan resulted in 7.5 fewer annual new drug discoveries on average from 1980 to 2003.[21]

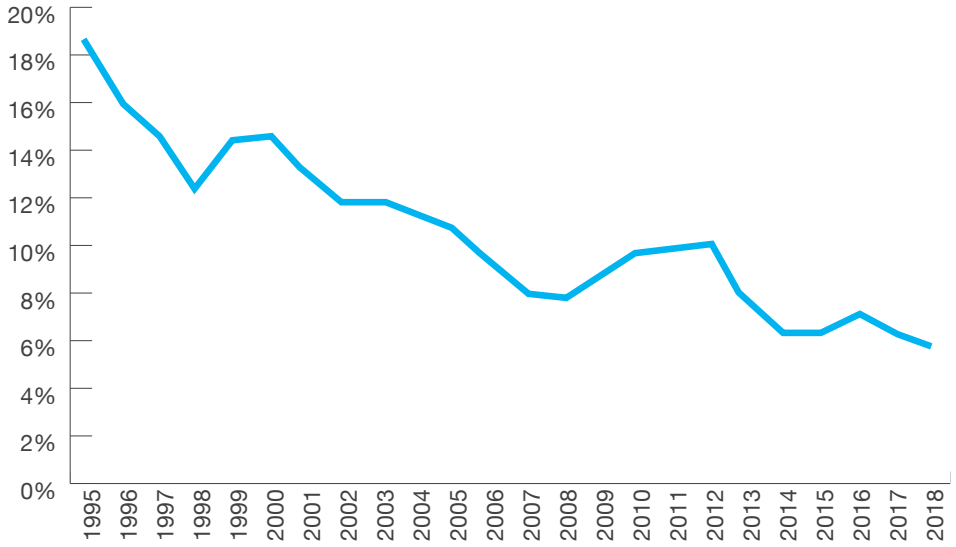
The potential revenue of developing a new drug in Japan was less than in other markets like the United States. Without the ability to recoup R&D investment, Japanese pharmaceutical companies opted to reduce investment in innovative new medicines and treatments. Without a pipeline of new medicines, pharmaceutical manufacturing production falls. From 1995 to 2018, Japan's share of global value added in the pharmaceutical industry declined by 70%, falling from over 18% to less than 6%.

Japan's challenging regulatory procedures and stringent price control regulations, which involve periodic reductions in prices, have posed significant obstacles for pharmaceutical companies engaged in the research and development of groundbreaking medications.[22] The effects of Japan's demanding regulatory framework and rigorous price control policies extend beyond the pharmaceutical industry, directly impacting the well-being of its citizens. The constraints imposed on pharmaceutical companies' ability to innovate and develop cutting-edge medications have led to a reduced availability of advanced treatment options for various medical conditions. This limitation has implications for Japanese patients who may have to contend with delayed access to novel therapies that could potentially enhance their quality of life or even extend their lifespans. Additionally, the reluctance of pharmaceutical companies to invest in Japan's market due to these hurdles can hinder the country's progress in becoming a hub for medical innovation, leading to missed economic opportunities and collaborations with global research endeavors.

GERMANY'S GARBLED GAMBLE

In 1992, a significant turning point occurred in Germany's pharmaceutical landscape with the implementation of the Health Sector Act and its accompanying stringent price regulations. The primary objective of these regulations was to curtail the rising healthcare costs and make medications more accessible to the general population. However, these well-intentioned measures had unintended consequences that reverberated through the pharmaceutical industry and innovation landscape in Germany.

FIGURE 1. JAPAN'S SHARE OF GLOBAL VALUE ADD IN PHARMACEUTICAL PRODUCTS



The regulation inadvertently created an environment that discouraged pharmaceutical companies from investing in R&D activities within the country. The stringent price controls placed limitations on the potential profits that companies could generate from their products, making it less financially viable for them to allocate resources toward innovative R&D endeavors. This financial disincentive, coupled with the uncertainty surrounding returns on R&D

investments, led to a noticeable decline in R&D initiatives within Germany's pharmaceutical sector.

The consequences of reduced R&D activities were felt across the industry. Between the years 1992 and 1999, approximately 23,000 jobs were eliminated within the German pharmaceutical sector. This marked workforce reduction, while reflecting cost-cutting measures by companies, also underscored the broader impact of the regulatory environment on employment and the economy. The job losses not only affected the pharmaceutical companies themselves but also related industries that supported the pharmaceutical sector.

By the turn of the century, Germany's pharmaceutical leadership had declined noticeably. Once a leading force in innovative pharmaceutical R&D in Europe, the country had slipped to third place by 2001.[23] This decline was not merely a shift in rankings; it symbolized a loss of Germany's competitive edge in a critical sector that had the potential to drive economic growth and improve public health.

While the intention behind the introduction of stringent price regulations was to strike a balance between affordability and innovation, the resultant negative impacts on R&D and industry competitiveness highlighted the complexities involved in regulating price in an R&D intensive industry. The case of Germany serves as a cautionary tale, demonstrating the delicate equilibrium that must be maintained between fostering a supportive environment for innovation and ensuring access to essential medications for the population. The German experience underscores the need for a comprehensive approach that considers the long-term implications of regulatory decisions on all aspects of the pharmaceutical ecosystem, from R&D investment to job creation and global competitiveness.

The Economic Contributions of the Pharmaceutical Industry

The pharmaceutical and medicine manufacturing industry is a vital component in the nation's healthcare system. The industry is also a significant contributor to the U.S. economy. Pharmaceutical and medicine manufacturing firms utilize cutting-edge technology and hire significant numbers of skilled workers to generate tremendous amounts of economic output.

Importantly, the pharmaceutical manufacturing industry helps support economic activity in addition to what is reported in official statistics. It operates in a unique supply chain that requires a diverse array of goods and services. Additionally, a portion of the income earned by workers is spent, generating further economic activity. These effects are known as indirect and induced impacts. To measure the total economic contribution of the pharmaceutical manufacturing industry, we use input-output (IO) analysis and IMPLAN, a widely used economic modeling system.

METHODOLOGY & KEY TERMS

The calculated economic impacts presented in this study make use of IO tools, also known as interindustry analysis. These tools can be used to estimate chains of effects that occur through the interrelationships between businesses, government, and households. This analysis uses the 2021 IMPLAN database and model. All economic impacts are presented as inflation-adjusted 2021 dollars. All results are for the 2021 calendar year. Appendix C provides estimates of approximate impacts attributed to the pharmaceutical and medicine manufacturing industry in 2023.

Three types of economic impacts are derived in this study:

1. Direct impacts—Activity generated within the focus industry. In this case, pharmaceutical and medicine manufacturing activity drives the direct impact.
2. Indirect impacts—Activity generated in other industries due to purchases (materials, energy, and services) by the focus industry through the supply chain. For example, an automobile manufacturing firm might purchase tires, steel, and electrical components to produce their final product.
3. Induced impacts—Activity generated by purchases of households from income earned from direct and indirect production.

This research estimates the direct, indirect, and induced impacts on the following:

1. Employment—People employed by an industry. Employment figures use the Bureau of Economic Analysis and the Bureau of Labor Statistics' full-time/part-time annual average for a given industry. The data cover both wage and salary employees and those who are self-employed.
2. Labor income—Labor income[24], a component of value added, is the sum of salary/wages and supplements. Supplements may take the form of employer contributions for employee pensions and insurance funds (such as health insurance) and employer contributions for government social insurance (social security). This concept also includes proprietor income.

3. Value added—Value added may be considered the industry's contribution to GDP and represents the enhancement a manufacturer provides (e.g., assembly) to a product before offering it to the end consumer. Put another way, value added is the difference between the total revenue of an industry and the cost of intermediate inputs. Components of value added include employee labor compensation, taxes on production and imports, and gross operating surplus (including profits).
4. Output—Output, in economic terms, refers to the total value of all goods and services in an industry. This includes both intermediate demand (sales of intermediate inputs to other industries) and final demand.

IO analysis shows the interrelationships between industries. These interrelationships are illustrated through tables. The column of a table provides all the inputs of other industries used to produce that industry's product. The table columns identify the industries and final uses that the industry sells to, and in sum, these tables are used to calculate the indirect impacts of a given industry's production.

For this analysis, the pharmaceutical manufacturing industry includes the following:

- Pharmaceutical and Medicine Manufacturing (NAICS 3254)
  - Medicinal and Botanical Manufacturing (NAICS 325411)
  - Pharmaceutical Preparation Manufacturing (NAICS 325412)
  - In-Vitro Diagnostic Substance Manufacturing (NAICS 325413)
  - Biological Product (Except Diagnostic) Manufacturing (NAICS 325414)

A multiplier can be viewed as the ratio of an impact or contribution over the original stimulus. For example, the multiplier of output would show the ratio of additional indirect and induced output generated, divided by the output of the focus industry. The larger a multiplier is for a given industry, the more efficient that industry is at distributing wealth throughout the entire economy.

Output measures include double counting. For example, the tire used to build a motor vehicle is counted both as the output of tires and the output of motor vehicles. This is important only if both are produced in the same study area. However, employment, labor income, and value added are additive, not double counted. Many slices of value added contribute to the final value of a product or service.

DIRECT IMPACTS

TABLE 2. PHARMACEUTICAL & MEDICINE MANUFACTURING, DIRECT IMPACTS SUMMARY

Units: Thousand Jobs and Billion $

This summarizes the direct economic impacts of pharmaceutical and medicine manufacturing and its subsectors. Total pharmaceutical and medicine manufacturing (NAICS 3254) activity contributes $192 billion in value added, accounting for 0.8% of U.S. GDP. The industry employs 291,000 persons. Pharmaceutical and medicine manufacturing employees earn $53.7 billion in labor income (sum of salary/wages and supplements). This equates to labor income of over $184,000 per worker.

NAICS INDUSTRY	Employment	Labor Income	Value Added	Output
325411 - Medicinal and Botanical Manufacturing	34.0	$5.6	$11.0	$22.3
325412 - Pharmaceutical Preparation Manufacturing	189.7	$36.5	$151.2	$280.4
325413 - In-Vitro Diagnostic Substance Manufacturing	29.9	$5.2	$10.3	$19.7
325414 - Biological Product (Except Diagnostic) Manufacturing	37.4	$6.4	$19.6	$32.0
3254 - Pharmaceutical and Medicine Manufacturing	291.0	$53.7	$192.0	$354.3

Productivity, measured as output per worker, is a fundamental driver of economic growth and global competitiveness. Several factors contribute to the pharmaceutical industry's high productivity. Strong capital investment and capital stock per worker directly elevate output. Similarly, R&D on a per-worker basis can foster innovation and efficiency, pushing productivity higher. The pharmaceutical industry often stands at the forefront of technological advancements, which can further streamline processes and enhance worker efficiency. The integration of advanced analytics and automation, for instance, aids in optimizing workflows and accelerating drug discovery and production. It's also worth noting that the collaborative nature of the sector, with its numerous partnerships between researchers, universities, and companies, often acts as a catalyst for sharing knowledge and best practices, further bolstering productivity levels.

Pharmaceutical and medicine manufacturing employees earn an average of more than $184,000 in labor income. This is roughly 2.5 times greater than the U.S economy's average labor income ($73,000). It is also greater than many high-paying industries such as finance and insurance ($100,000); professional, scientific, and technical services ($109,000); and management ($146,000).

FIGURE 2. OUTPUT PER WORKER
Units: Dollars

FIGURE 2 illustrates the industry's labor productivity. The aggregate pharmaceutical and medicine manufacturing industry generates more than $1.2 million in economic output per worker. This is nearly six times greater than the U.S. economy's average output per worker ($208,000).

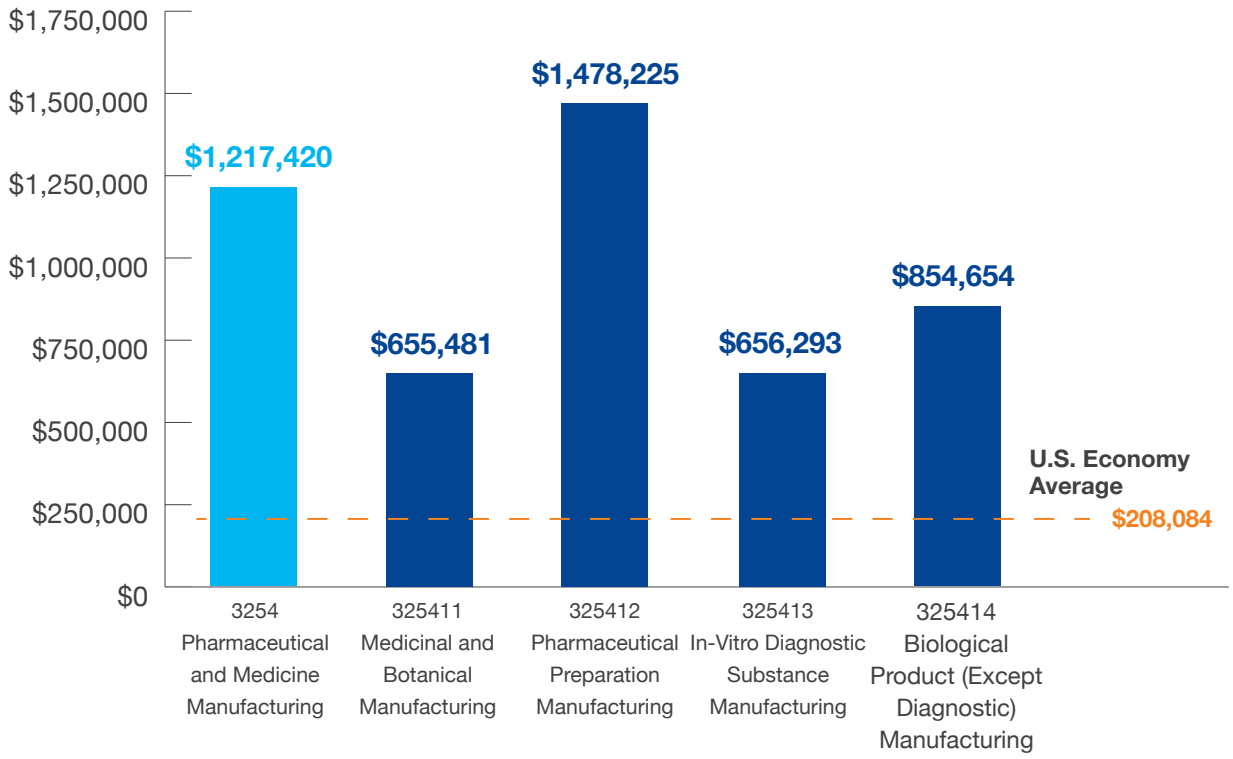
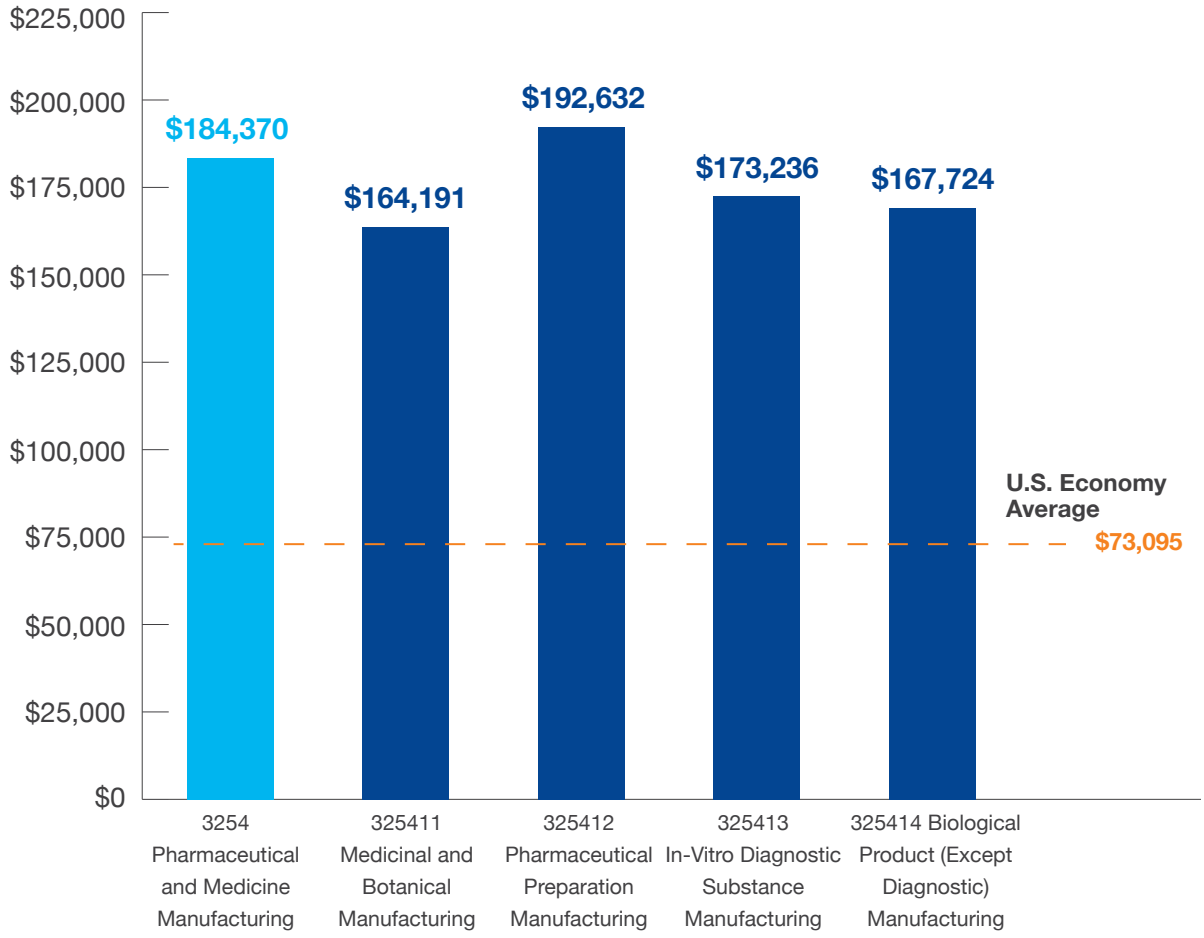


FIGURE 3. LABOR INCOME PER WORKER

Units: Dollars



INDIRECT & INDUCED IMPACTS

The impact of the pharmaceutical and medicine manufacturing industry extends beyond the direct economic impacts described in the previous section. Output and jobs are also supported in supplier ("indirect") industries that provide components, materials, energy, and various services to the industry. Additionally, individuals employed by manufacturers and the associated supply chains earn income. A portion of these funds is used to purchase consumer goods and services, helping create jobs and support other industries. These impacts are known as induced effects.

A Conversation with FRITZ BITTENBENDER

Senior Vice President, Public Affairs & Access, GENENTECH

What are the characteristics of economies that have vibrant pharmaceutical sectors?

Economies with vibrant pharmaceutical sectors typically exhibit some important traits, each of which is indispensable to ensure all aspects of drug development can thrive, patients get access to effective medicines at the right price and the right time, and financial incentives are aligned in a way that allows for companies to continue focusing on innovation and being able to meet population needs.

A robust framework of intellectual property protection and ensuring that innovation is rewarded and incentivized is the basic hallmark of a strong pharmaceutical sector. A skilled and specialized workforce drives research, development, and manufacturing excellence. The presence of a sophisticated healthcare system ensures that novel treatments reach patients efficiently, while transparent and sustainable pricing mechanisms balance accessibility with the need to fund future innovation. Furthermore, a collaborative ecosystem involving academia, industry, and regulators fosters continuous advancement and growth.

What are you most excited about in the pharmaceutical industry right now?

Precision medicine and personalized therapies are revolutionizing healthcare with treatments tailored to individual genetic profiles, leading to enhanced patient outcomes. These targeted treatments not only improve efficacy but also reduce side effects. Advanced drug delivery systems, using nanotechnology and biodegradable polymers are enhancing targeted drug delivery, minimizing systemic toxicity and maximizing therapeutic efficacy. The healthcare sector is also witnessing the rise of digital therapeutics integrated with AI. These are non-drug interventions delivered digitally to manage diseases. AI-driven analytics are enabling patient monitoring and early interventions.

Decentralized clinical trials, facilitated by remote patient monitoring and telemedicine are allowing diverse patient participation and robust real-world data collection. Cell and gene therapies have the potential to revolutionize healthcare. CRISPR and other gene-editing technologies are paving the way for curative treatments, and therapies like CAR-T show promise in oncology and rare diseases. A few more areas are microbiome therapeutics, biosimilars and complex generics, and collaborative R&D models.

What are some of the biggest risks to the sector right now?

Some of the most significant risks to the healthcare sector currently include regulatory challenges, evolving drug approval standards for novel therapies, and intense scrutiny on drug pricing by governments. There are also concerns regarding pricing pressures, reimbursement issues, and challenges in securing reimbursement for high-cost treatments. The industry faces threats from patent cliffs, loss of exclusivity for major drugs, and increasing competition from generics and biosimilars. Supply chain vulnerabilities, high attrition rates in drug development — particularly in late-stage trials — and escalating R&D costs without assured success further compound these risks. Additionally, the sector must navigate a rapidly changing landscape with new entrants, disruptive technologies, and shifts in healthcare policies, notably in major markets like the United States.

Pharmaceutical and medicine manufacturing directly employs 291,000 people, generates over $192 billion in value added, and contributes over $354 billion in output. These numbers can be seen in the first row of Table 3. It is worth noting that these are all significant increases from 2019. Employment has risen approximately 9% in the last 24 months. Economic value added generated by the pharmaceutical industry has risen a whopping 24% in just the last 2 years.

Direct activity helps generate indirect activity within the economy. These upstream suppliers, who provide inputs for manufacturers, employ just under a half-million people and support over $160 billion in economic output. Finally, a portion of the labor income earned by workers in the pharmaceutical and medicine manufacturing industry and their supply chains is spent on goods and services. This activity, seen in the third row of Table 3, supports nearly 704,000 additional workers and generates nearly $80 billion in value added. In total, pharmaceutical and medicine manufacturing activity helped contribute almost 1.5 million jobs, $147 billion in labor income, $355 billion in value added, and $655 billion in economic output.

Economic multipliers describe the ratio of the sum of indirect and induced impacts to direct impacts. The data shown in Table 3 indicate that one pharmaceutical

TABLE 3. PHARMACEUTICAL & MEDICINE MANUFACTURING (NAICS 3254) TOTAL IMPACTS

Units Indicated

	Employment (1,000 Persons)	Labor Income (Billion $)	Value Added (Billion $)	Output (Billion $)
Direct	291.0	53.7	192.0	354.3
Indirect	495.6	48.0	82.5	160.4
Induced	703.7	45.6	79.9	140.5
Total	1,490.3	147.3	354.5	655.2

and medicine manufacturing job helps support 4.1 other jobs in the economy.[25] Additionally, one dollar of the industry's output generates $0.85 of output elsewhere in the economy.[26]

As previously mentioned, the activity of pharmaceutical and medicine manufacturing companies drives business in industries upstream in the supply chain. This activity is summarized through IO tables that numerically describe the sales and purchases relationships that exist between producers and consumers in an economy. By analyzing these tables, we can pinpoint the group of secondary industries that experience the greatest benefits from pharmaceutical and medicine manufacturing, considering factors such as supported employment and generated output.

FIGURE 4. U.S. PHARMACEUTICAL & MEDICINE MANUFACTURING (NAICS 3254) TOTAL IMPACTS

Units Indicated

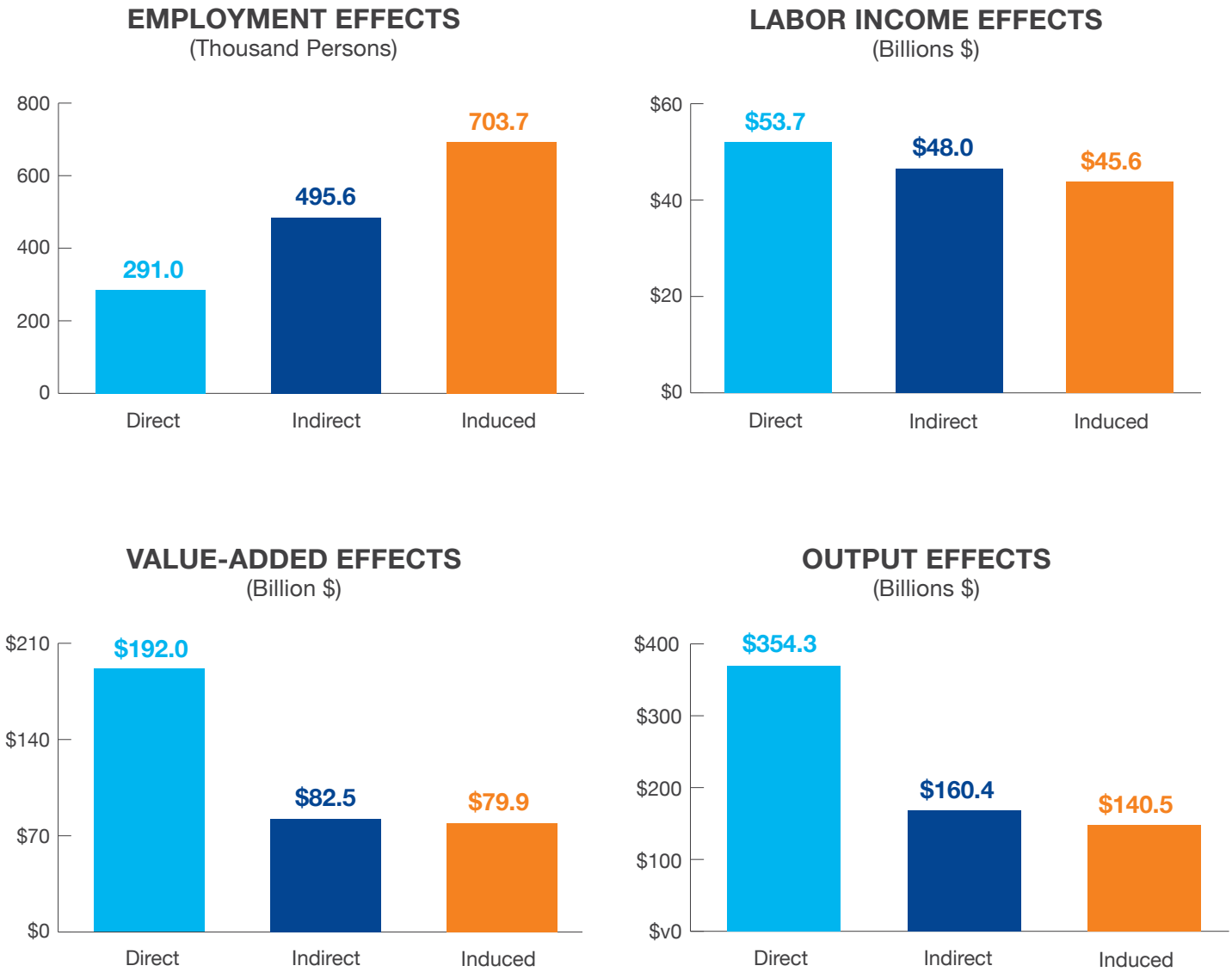


TABLE 4. INDIRECT EMPLOYMENT – TOP 10 INDUSTRIES

Unit: 1,000 Persons

This table describes indirect employment impacts by detailed industries. The largest affected industry is 'Management of companies and enterprises' (57,700 jobs). This industry helps support manufacturing firms by assisting in strategic or organizational planning. The second-largest industry, 'Wholesale – Drugs and druggists' sundries' (40,300 jobs), supports the distribution of biological and medical products. Other top affected industries include 'Employment services' (21,500 jobs), 'Other real estate' (19,200 jobs), and 'Couriers and messengers' (17,300 jobs).

INDUSTRY	Indirect Employment
Manufacturing of companies and enterprises	57.7
Wholesale – Drugs and druggists' sundries	40.3
Employment services	21.5
Other real estate	19.2
Couriers and messengers	17.3
Truck transportation	16.5
Management consulting services	14.5
Advertising, public relations, and related services	14.3
Warehousing and storage	13.0
Business support services	11.6
All other industries	269.8
TOTAL INDIRECT EMPLOYMENT	495.6

TABLE 5. INDIRECT OUTPUT – TOP 10 INDUSTRIES

Unit: Billion $

This table highlights indirect output impacts by detailed industries. This list of industries is similar to the indirect employment in Table 4 but includes some unique sectors. Differences between Table 4 and Table 5 are due to varying labor productivity across industries. For example, industries that supply high-value (and relatively low labor intensity) feedstocks such as 'Other basic organic chemical manufacturing' ($4.1 billion) and 'Petrochemical manufacturing' ($3.0 billion) are featured.

INDUSTRY	Indirect Output
Wholesale – Drugs and druggists' sundries	34.7
Management of companies and enterprises	15.4
Internet publishing and broadcasting and web search portals	6.2
Other real estate	4.2
Other basic organic chemical manufacturing	4.1
Wholesale – Other nondurable goods merchant wholesalers	3.8
Advertising, public relations, and related services	3.3
Truck transportation	3.2
Petrochemical manufacturing	3.0
Employment services	2.5
All other industries	80.1
TOTAL INDIRECT OUTPUT	160.4

A Conversation with KARIN SHANAHAN

Executive Vice President Global Product Development & Supply, BRISTOL MYERS SQUIBB

What is the impact of pharmaceutical price controls, like those in the IRA, on the broader pharmaceutical industry?

At Bristol Myers Squibb, we are concerned about the impact the so-called "negotiation" program in the IRA is going to have on clinical research and drug development. The real victim of the program will be future innovation — and, in turn, the millions of patients who are counting on the pharmaceutical industry to develop new treatments and cures.

What areas of the industry will be most severely impacted by the IRA's provisions on drug pricing?

We think it will be felt most acutely in oncology. In our industry, the majority of cancer research happens after a drug's initial U.S. Food & Drug Administration (FDA) approval, when we seek to better understand the effect of a medicine on different patient populations, other types of cancers, and earlier stages of disease, so that we can help more patients. Bristol Myers Squibb has led profound advances in the treatment of cancer, making long-term survival a possibility for more patients. However, our focus is on the job that we still have left to do, and the so-called "negotiation" program puts future oncology research and progress at risk.

How will price controls impact R&D (e.g., potential impact to investment in small molecule medicines)?

The IRA policies have already changed the way we look at our development programs in oncology and beyond, whether it's a decision to advance a new medicine or pursue additional indications for an existing one. These are difficult decisions when we know much of our progress against cancer, in particular, is the result of post-approval research.

Which pipeline projects are likely to be most negatively impacted and why does that matter (e.g., new medicines planned but not yet in clinical development and/or treatments for specific diseases)?

It is going to be harder to develop medicines for newly diagnosed patients in the first-line setting because of very lengthy trial requirements that can take 8 to 10 years. I know that we've shared the difficult decision not to pursue a registrational study of a molecule called iberdomide in newly diagnosed multiple myeloma patients, given these dynamics.

When would you expect to see these impacts materialize and how are the short-term impacts, different from the long-term impacts?

Pharmaceutical manufacturers have to start operating now on the expectation that our most innovative and successful products are going to be subject to the IRA's policies. While we will never stop working for patients, we are already having to make tough decisions. This reality will only grow more pronounced as implementation of the IRA moves forward.

What are you most excited about in the pharmaceutical industry right now?

There is a lot to be excited about in the pharmaceutical industry right now, but advances in manufacturing technology enabled by artificial intelligence (AI) and machine learning, as well as other technologies, such as autonomous equipment and flexible manufacturing design are disrupting the industry and helping us deliver treatments to patients with more agility. Collaboration with the

FDA to develop high-efficiency manufacturing for complex therapies is another exciting development area, as is the adoption of modular, portable, and sterile manufacturing suites that will one day enable manufacturing at hospital sites to achieve "point of care" manufacturing, while prioritizing GMP and other key criteria. Point of care manufacturing can be useful for advanced therapies derived from techniques such as gene editing, cell manipulation, and tissue engineering.

In addition, I believe that there is significant untapped potential in generative AI, and digital more broadly, across biopharma, including in R&D, manufacturing, and commercial. AI and digital have tremendous potential to help accelerate drug design, early-stage drug discovery, and the generation of clinical evidence, with the potential to reduce the development process from 4 years to 8 months and decrease the total time to bring a new molecular entity to market from 13 years to 6 years. In biomanufacturing, there is the potential to enhance product yields and reduce manufacturing equipment down time.

What are some of the biggest risks to the sector right now?

Supply disruption continues to be a big risk to the sector, and is driven by factors such as geopolitical instability, material shortages from active pharmaceutical ingredients (API) to semiconductors, as well as skilled labor shortages. COVID shined a light on many pharma companies' lack of operational resilience, as API shortages, transportation challenges, and staffing issues resulted in shortages of many common medicines. The industry can do better in terms of quickly identifying and assessing the risk of potential disruptions, reacting faster when they do occur, and recovering from the impacts of these disruptions across the end-to-end (E2E) supply chain. Although we didn't have major COVID-related disruptions to our supply chain at Bristol Myers Squibb, it is an area that we continue to invest in for the future. It's imperative for pharma companies to develop robust resilience capabilities across the life cycle and value chain to not only ensure operational and financial success, but also better position us to meet the needs of the patients who count on us.

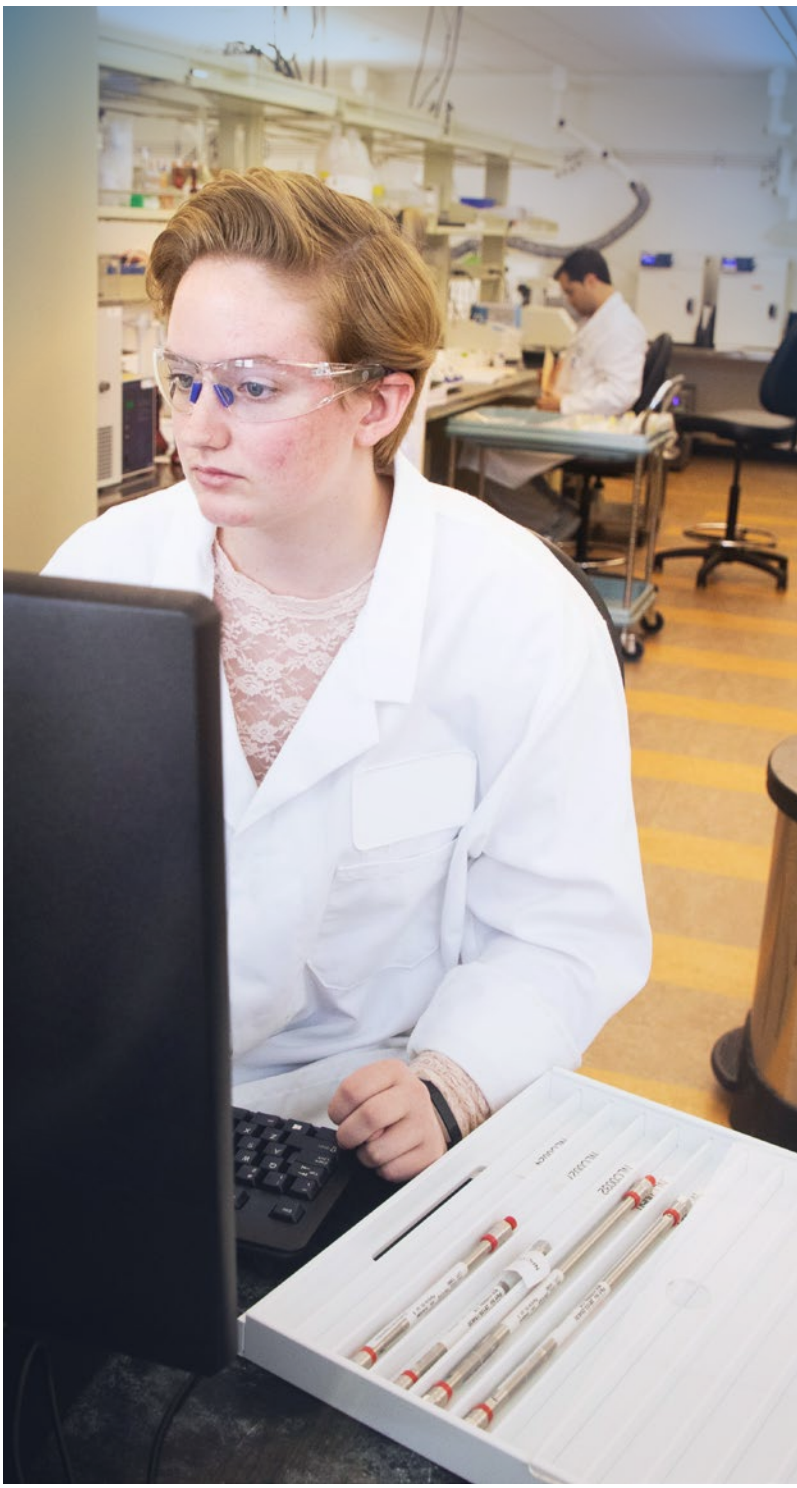
As noted earlier, policies such as the IRA are already having an adverse impact on our ability to bring innovative medicines to patients, and we anticipate this negative impact to increase over time.

How Price Controls, Like Those in the IRA, May Hurt U.S. Pharmaceutical Leadership

President Biden signed the IRA into law on August 16, 2022. The law is designed to lower prescription drug costs in Medicare through three provisions: government negotiations of Medicare drug prices, penalties on Part B and Part D medicines that experience price increases in excess of inflation, and amendments to the design of the Part D benefit.

The IRA requires pharmaceutical companies producing high-expenditure drugs under Medicare to negotiate prices with the Department of Health and Human Services. The process started in 2023 with the selection of the first 10 Part D drugs that will be subject to negotiations; the price caps will go into effect in January 2026. The IRA is already having negative consequences on R&D investment for crucially needed treatments as impacted biopharmaceutical companies prepare for implementation of this consequential legislation. For example, Alnylam Pharmaceuticals announced it would not initiate a phase 3 study aimed at addressing a rare eye disorder, citing IRA.[27] AstraZeneca has said the IRA could potentially lead to delayed drug releases for new medicines in the United States and a shift in R&D.[28] Bristol Myers Squibb noted they were likely to cancel some R&D programs as a result of the IRA.[29]

Over time, more medications will be eligible for price negotiation, but newer drugs are initially exempt. According to the law, small-molecule drugs, which are often administered in pill form, are exempt from negotiation for 9 years, while large-molecule biologics, which are usually administered through injections or infusions, are shielded from negotiation for 13 years. This glaring inconsistency in the law differentiates the intellectual property value of the medicine by separating the classes of medicines and will have long-term consequences on the medicines available in the U.S. One of the biggest potential negative consequences is a result of the IRA's unequal treatment of small molecule medicines and biologics discussed in more detail in the following section.

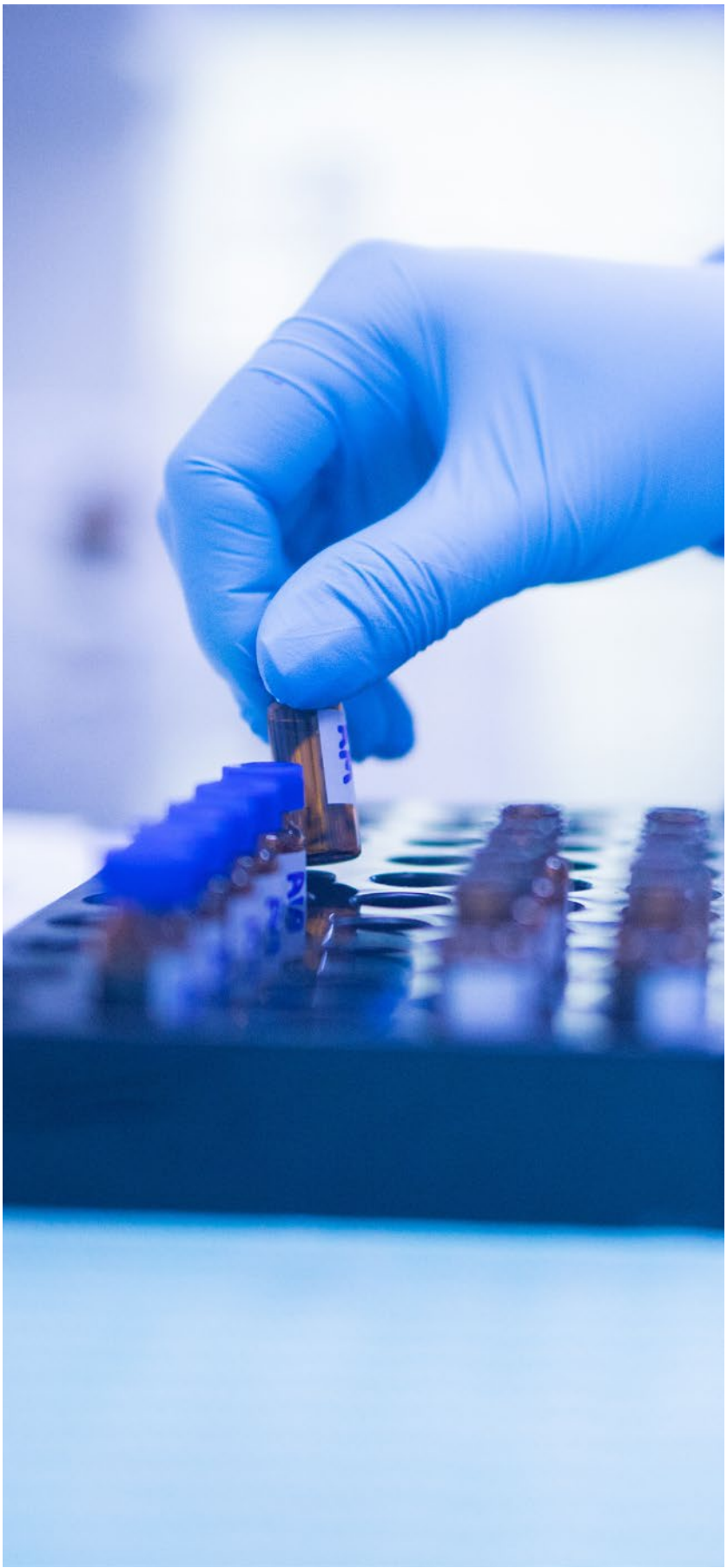


The IRA will have detrimental effects on the leadership and economic viability of the pharmaceutical industry. The law will inadvertently hinder the industry's ability to innovate, invest in R&D, and maintain its position as a global leader in pharmaceutical innovation.

One of the critical repercussions of the act is the potential erosion of financial resources available for R&D. As already noted, the pharmaceutical industry relies heavily on substantial R&D investments to develop new drugs, therapies, and medical breakthroughs. By distorting existing market forces, the law diverts crucial funds away from R&D efforts, crippling the industry's capacity to pursue cutting-edge research and innovation. Furthermore, the uncertainty created by the IRA discourages investments. This, in turn, hampers the industry's ability to bring new life-saving treatments to market, negatively impacting public health outcomes.

The negative economic consequences of the IRA are also significant. The pharmaceutical industry contributes significantly to job creation, economic growth, and overall economic output. Disrupting existing market dynamics strains industry's ability to invest, which can lead to job losses and a decline in industry dynamism. Ultimately, these consequences have far-reaching effects on the economy as a whole, including decreased tax revenues and potential long-term damage to the nation's competitiveness in the global pharmaceutical market.

While the intention of the IRA is to address rising costs, its application to the pharmaceutical industry will have unexpected consequences. Striking a balance between preserving the law's objectives and safeguarding the long-term viability and leadership of the pharmaceutical industry is crucial. Policymakers need to carefully consider the potential impact of the law on the industry's R&D efforts, investment landscape, and overall economic contributions to ensure that the pharmaceutical sector can continue to drive advancements in healthcare and play a vital role in the nation's economic prosperity.



SPECIFIC RISKS TO SMALL MOLECULE MEDICINE INNOVATION

The process of manufacturing a new drug from conceptualization to product launch can require 12 to 15 years and cost more than $1 billion. In order to make this type of substantial investment, pharmaceutical companies need to recoup their initial investment. Elements of the IRA create uncertainties that are likely to further curb R&D investment.

The IRA requires the federal government to negotiate prices for some drugs covered under Medicare. The medicines eligible for negotiation are brand-name and biologic medicines without generic or biosimilar equivalents covered under Medicare Part D or Part B. The medicines must be among the highest-spending Medicare-covered drugs and are 9 or more years past FDA approval for small molecule medicines or 13 or more years for biologicals.

The uneven treatment of the two classes of medicine will likely result in less drug development of small molecule medicines because of more limited protections from the implications of the IRA.

At Lilly, for example, 40% of the company's overall portfolio is small molecule treatments. Vitally, the majority of its oncology pipeline is made up of small molecule treatments because many types of cancer can only be addressed using small molecules. Already, Lilly has discontinued development of a treatment for certain blood cancers after assessing the impact of the law in conjunction with other factors. As Lilly CEO Dave Ricks noted, "the difference between a 9- and 13-year product line is about 50% or 60% of the value. In 10 years, we'll have far fewer small molecules being developed than we do today."[30]

The majority of medications currently available are small molecules. These compounds are orally administered, can readily be absorbed into the bloodstream, and have the ability to easily permeate cell membranes. Examples include aspirin, statins employed for treating high cholesterol, and blood pressure drugs. But pharmaceutical companies are also currently working on small molecule medicines for diseases that currently only have injection or infusion options. As Lilly CEO Dave Ricks notes, the law establishes "rules that really just disincentivize investment in what ends up being convenient drugs, drugs for tough conditions like cancer, and drugs that get really cheap when they go generic."

If small molecule medicines had parity with biologics this would create a more level playing field, which would more fairly incentivize the development of new and innovative treatments, ensuring patients can access the most effective treatments.

Pharmaceutical Manufacturers Are Already Curtailing R&D Efforts

Pharmaceutical manufacturers have already cut certain R&D efforts as a result of the financial implications and investment disincentives of the IRA and have specifically cited the IRA as the disincentive to continuing these efforts. Curtailing R&D efforts will negatively impact investment in medications to treat both chronic conditions as well as rare conditions, leading to a rise in negative healthcare outcomes and expenses nationwide.

Alnylam Pharmaceuticals announced it has suspended plans for a phase 3 trial to assess vutrisiran for the treatment of Stargardt disease, a rare eye condition. Lilly announced that it has terminated the development of a phase I drug licensed from Fosun Pharma. The LOXO-338, a BCL2 inhibitor, was being investigated to treat several types of blood cancers, but that research program was ended because of the negative impact the IRA has on small molecules in oncology.[31]

A Conversation with DR. FRANK SCHOLZ

President & CEO, NORTHSTAR MEDICAL RADIOISOTOPES

What makes the U.S. market special when it comes to pharmaceutical manufacturing?

There are certain things the U.S. market has that other markets have as well. These include a strong regulatory framework, stability, and safety standards. The comparative advantages of the United States are, first, the reimbursement for investment and, secondly, the size of the market. Pharmaceutical manufacturers want the United States to be a viable market for R&D and production because of the large size of the addressable market. Patients are always number one on the mission statement.

If you look globally, pharmaceutical manufacturers select markets, or deselect markets, based upon hurdles, costs, and time-to-market restrictions.

In the United States, there are concerns that growing regulatory hurdles will potentially slow the introduction of innovative drugs. You can destroy a market by introducing measures that lower innovation or otherwise restrict companies from earning revenue that fuel future research expenses and fund innovation. And that's because the environment has changed the regulatory environment in a broader sense.

What are the biggest risks facing the U.S. pharmaceutical industry?

I think the biggest risk is that we are spending a big portion on non-value-add parts of the value chain. For example, the healthcare system is spending a lot of money on PBMs (pharmacy benefit managers). The share of the profit pool that is taken away by the PBMs returns zero to very little value-add to patients or to the market. The spend is a burden and you have to allocate it to the best use, which is providing treatment to patients.

If you think about how much PBMs and health insurance take from the pool relative to what they add, that's just not in the interest of patients, and I think it's economically misaligned. That means the outcomes are suboptimal.

Drug manufacturers are often criticized for high drug prices, but if you actually follow the drug pricing from list price to discount to what is being charged to patients, you can clearly prove that the problem of too high prices comes from other parts of the value chain. I think this is the number one task for us to correct.
We need to allocate it better and then we will have better outcomes for the country.

What drives the cost of new medicines?

We are pushing into harder-to-treat diseases and diseases that have small incident rates. You have a higher cost of entry into certain areas of new medicines and more specialized treatments require higher costs. This is always the case of the innovation cycle. The more precise you are, the more you come with a different absolute amount of variable costs in these therapies.

What does the future of the pharmaceutical industry look like?

We will have quite a bit of highly innovative drugs coming into the market pretty soon. Think about cell gene therapy and radiopharmaceuticals and everything that runs under the umbrella of precision medicine. This will be terrific for patients, but it will be expensive to introduce these life-prolonging, or potentially life saving therapies to market, and it will be very difficult to attract companies if the market does not provide a return that enables companies to recoup these high expenses. If we do not provide appropriate funding and appropriate management, then we will be slow, we will be behind, and we will just let people die earlier because every month you are late with a certain therapy, people will just not make it. So you have an economic component but you also have a very personal component as well.

A Conversation with JACOB VAN NAARDEN

President, LOXO@LILLY
Executive Vice President, LILLY

What do you think is being missed in the current conversation about price controls?

Pharmaceutical manufacturers invent things. Usually, they are things that are not difficult to copy from a technical standpoint. In other words, once you know the chemical structure of a molecule, it is usually not that hard to figure out how to make it. So the patent system protects people from doing that. The industry has the incentive to invest in R&D because they understand the predictable timelines of when they have a medicine that they can have a branded price and recoup those large R&D investments and also a clear understanding of when that is going to go away. We have lost that thread in this entire conversation.

Countries that have done over-the-top pricing control have seen their pharmaceutical industries weakened. They do not have, for the most part, in-country ecosystems of innovation. They take innovation mostly from the United States – that's not exclusively true, but mostly true. And they get access to medicines much later in the medicine's life cycle and, in some cases, not at all. Patients are not really benefiting from that though the motivation for price controls was to help patients.

There is another avenue of this that is not about the price but about the patients' out-of-pocket expenses, and that remains a big problem in the United States. Is that a pharmaceutical price problem? Or is that an insurance-design problem? I would contend it's the latter.

The out-of-pocket component in the U.S. healthcare system is the real problem, especially for specialty medicines. But I don't think that the pricing dynamic is the core issue because changing it would not actually solve the problem.

How do changes to the patent system impact innovation in the United States?

Take a step back and look at how many unbelievably effective medicines, that have had huge impacts on public health over the course of our entire industry, are now available for pennies. This is amazing. That is the system working.

There are two vital components. First, the period of exclusivity, whether it's patent exclusivity or pre-market pricing, needs to be long enough to allow pharmaceutical industries to recoup the R&D investment on a probability-adjusted basis knowing that a lot of projects are going to fail. Secondly, the system needs to be predictable. Both of these are very important. When governments choose for political reasons to change the former, it creates a problem in the latter. It is not just the fact that the time frame is changing, but also the predictability changes.

In the pharmaceutical industry, we are making investments based on 7 to 10 year time frames for any given medicine. That is a long time frame, and when you don't know what your time frame is or it changes midstream, that is very dramatic. It is very hard to plan and very hard to know how to invest when you do not really know what your time frame is.

Can you give examples of how changing the patent system negatively affects medicine innovation?

There are two examples in our portfolio right now that I think would have played out differently. These are both small molecule cancer drugs. The first is a medicine called Verzenio that is currently approved for a couple different settings of breast

cancer and we hope soon to be approved for the treatment of a certain type of prostate cancer.

Cancer drugs are typically first tested in the sickest of the sick patients, and the main reason for that is because the industry has come a long way in combating cancer, and there are standards of care in earlier lines of therapy. With a new medicine, you generally end up testing with patients who have mostly failed a variety of other treatments. You first figure out if the new medicine works and move up over time.

In the case of Verzenio, we first tested the medicine in patients who had metastatic breast cancer who had already been through and progressed on their first therapeutic regimen. We then ran another trial in patients who were newly diagnosed with metastatic breast cancer who had yet to be treated at all. We then ran a third trial in what is called the adjuvant setting. In this setting we are targeting cancer cells that primary treatment did not destroy in order to lower the risk that the cancer will ever come back. In this stage we are trying to cure people, which in cancer, unfortunately, we actually do not have the opportunity to do all that often because so many cancers are diagnosed once they are actually incurable. When you can cure a person, that's unbelievable, and so we ran this incredibly large incredibly long study that read out positive and is, by far, the biggest impact setting of this medicine.

Would we have run that trial in a world in which our timeline was only 9 years? I don't know. That trial was read out in 2020 and did not get approved until late 2021. This was the biggest investment of the entire program with over 5,000 patients, which is a very big study for oncology and took 5 or 6 years to read out. I don't know that we would run that study if we only had a couple years to recoup the investment.

The prostate cancer program for the same medicine will not see the first trial read out until the end of 2023 or maybe the beginning of 2024. Could we have done that in this framework? No way. It destroys me to say that out loud because I'm not here doing this job for the profit-making of it. I don't think any of us are. We are here to transform the lives of patients living with devastating diseases, but in order to continue to do this long into the future we need to recover the cost of the investment.

The second medicine is Jaypirca, which received its first approval in 2023. It was developed to treat certain types of leukemia lymphoma. There is a type of leukemia called mantle cell lymphoma which is not common but is really horrible. Most patients relapse after their first treatment regimen unfortunately. In the context of exploring our medicine in clinical trials, we saw that the drug was working and the doctors working on the study suggested we start talking to the FDA. The incident rate is very low, and there is little business rationale in this particular disease setting. We are talking about maybe a thousand patients in the U.S. It is incredibly uncommon. But their outcome is really bad and our new medicine seemed to be working there. In the meantime, we

were working on a suite of larger studies in other forms of leukemia lymphoma that were much bigger opportunities — both on a business side as well as for patient impact. But these trials were going to take a long time to read out. Many of these studies will not be completed for many years.

With a shortened clock that only starts once the drug comes to market, companies are facing an impossible choice. We don't want to make these types of decisions. In a world in which we had more time on the clock, we wouldn't have to.

Why are shorter timelines especially impactful to oncology?

What typically happens in most disease settings outside of oncology is that green light investment in your program and you run the full suite of trials all at once. When you come to market you are coming to market with the full data package and all of your disease settings. What happens in oncology is a staged approach. We start with the most advanced patients and over time move into less advanced patients. That process takes years. Because of the way in which these trials work. The earlier stage trials take longer.

Timelines are long. Nine years is not enough time, particularly in oncology. It creates a dynamic challenge. We should not be forced into making decisions simply because we do not have enough time. If we aligned small molecules and biologics at 13 years, then I think we would all live with that, but nine is just not enough time.

What is next for oncology?

There is a lot of value, even though it is very difficult to quantify, in a patient living longer. Getting to experience those moments with their families and friends and doing so, with a good quality of life. Over time, every advance builds on the prior advances. In oncology, we have made unbelievable strides over the past 10 to 15 years — some by individual medicines and some by the series of medicines that have added on top of each other. That's what our industry has been very good at. We should be proud of that.

This is especially true when it comes to quality of life. The first wave of new oncology medicines 40 or 50 years ago might have worked, but the quality of life was horrible. They were so toxic. We have done a much better job of changing that tolerability safety versus efficacy quotient really over the past 10 to 15 years.

We are embarking on the next wave of oncology innovation. The first wave was the chemotherapy era. It is a really toxic drug. The second wave was the learnings from the Human Genome Project applied to cancer and biologic ideas based on genetics. A lot of that has now been harvested and has really impacted the lives of cancer patients in a positive way.

We are now embarking on the next journey, which is the next wave of biology insights. This will probably be harder than what we just experienced over the past 20 years. Anytime you make that much progress in a period of time, the next leg of progress is always going to be harder because you have to build on that.

This next wave is going to require more investment at lower probability of success because the biology that we are trying to address is just getting harder. The medicines we are trying to make are harder to discover. Secondly, we have to run bigger and larger studies to improve standard of care over the significant increase we have produced over the past 10 to 15 years.

The next era of innovation will require longer, bigger, more expensive, clinical trials. We are prepared to do that but we need to understand the regulatory environment and the rules have to make sense.

Can you explain why the time mismatch of the IRA matters?

In oncology most of the things that we end up wanting to address put us down the small molecule path. If at a macro level the world is saying biologics are more valuable, it is going to take investment away from oncology.

Addressing Chronic Conditions

Some 90% of the nation's $4.1 trillion in annual healthcare spending is for patients with chronic and mental health conditions according to the Centers for Disease Control and Prevention.[32, 33] Chronic conditions such as diabetes, cancer, and heart disease account for a significant portion of the total spend and are accompanied by immense economic cost, amounting to more than $216 billion annually for healthcare systems and resulting in billions in lost productivity on the job.[34]

As the U.S. population ages, the number of Americans suffering from chronic diseases is expected to increase significantly. The population of individuals aged 50 and above in the United States is projected to jump by over 61%, rising from 137.25 million in 2020 to 221.13 million in 2050. Within this group, the number of people suffering from at least one chronic ailment is anticipated to surge by 99.5%, climbing from 71.52 million in 2020 to 142.66 million by 2050.[35]

Pharmaceutical manufacturers are increasingly focusing on treatments for chronic diseases. Today, there are nearly 800 chronic disease medicines in development.[36] But the intricate characteristics of chronic illnesses create considerable obstacles in crafting effective treatments. Diseases like cancer, diabetes, and cardiovascular disorders can encompass numerous subcategories. Each of these subcategories may exhibit distinct molecular triggers and clinical results. Creating medications that span all subtypes or disease stages is costly and time consuming. Developing effective cures will require significant investment.

Annually, more than 1.7 million Americans are diagnosed with cancer, and nearly 600,000 die from it each year, making it the second leading cause of death in the United States.[37] Estimates suggest that by 2030, medical expenses related to cancer care will exceed $240 billion dollars.[38] Today, nearly 50% of the total FDA pipeline is for new cancer treatments, and more than a quarter of all new drug and biological approvals are for cancer.[39]

In 2022, President Biden reignited the Cancer Moonshot, setting an ambitious goal to reduce the cancer death rate by 50% over the next 25 years.[40] To accomplish this goal, the President's budget reflects an increase in cancer research funding. Assuming the rise in cancer research funding for the fiscal year was made permanent, it would result in an annual growth of approximately $1.9 billion, which represents roughly 3.4% of the present $56.8 billion combined public and private expenditure on cancer

R&D. Researchers at the University of Chicago found that price control measures in the IRA will reduce overall annual cancer R&D investment by about $18 billion, or nearly 32%. This reduction in cancer research is more than nine times larger than the amount of investment allocated by the President's budget.[41] In other words, nine times as many new cancer treatments will be lost by IRA provisions than will be gained by the President's investments in research. The IRA in turn will compete with the ambitious plans of the President's Cancer Moonshot.

Alzheimer's disease affects about 5.7 million Americans, including one in 10 adults aged 65 and older. In 2020, the estimated cost of caring for and treating people with Alzheimer's disease was more than $300 billion. By 2050, these costs are projected to exceed $1.1 trillion.[42]

Some business leaders and government officials have been quick to declare an end to the COVID pandemic. But, as World Health Organization Director-General Tedros Ghebreyesus noted, "no one is safe until everyone is safe." This includes those who suffer from COVID over an extended period of time. Data from the Census Bureau's Household Pulse Survey show more than 40% of adults in the United States reported having COVID in the past, and nearly one in five of those (19%) are still suffering symptoms of "long COVID." Long COVID also carries with it massive economic implications. By some estimates, as many as 4 million workers are out of work because of long COVID.[43]

Despite significant advancements in recent years, the pharmaceutical industry still has much to do. To stem future spending on chronic diseases and improve patient outcomes, there is a need for new treatments that go beyond the current standard of care. The future of pharmaceuticals will play a vital role in treating chronic conditions to ensure people can lead healthy lives.

Next Steps

At its core, the U.S. pharmaceutical industry thrives at the vital nexus between investments in R&D and strong IP protection. It is no secret that revenue serves as the lifeblood of innovation, driving the discovery, development, and delivery of life-saving medicines. Industry revenue paves the way for new drugs to emerge, offering hope to countless patients worldwide. Conversely, declines in revenue signify not only a missed opportunity for progress but also a potential setback in our collective fight against disease and suffering.

To put this into perspective, let us consider the remarkable commitment to R&D demonstrated by the pharmaceutical industry. This industry invests more in R&D than any other sector in the United States, even surpassing the remarkable intensity seen in electronics industries like the semiconductor industry. As we witness renewed efforts to strengthen the semiconductor industry, it becomes clear that a similar focus must be directed towards preserving and enhancing the resilience of our pharmaceutical sector.

But the story does not end there. To fully comprehend the dynamics at play, we must also explore the geographic environment within which the U.S. pharmaceutical industry operates. Pharmaceutical companies strategically choose locations where they can protect their intellectual property, recoup their substantial R&D investments, and ensure the continuous flow of life-changing medicines. The pharmaceutical industry is portable. As we have seen play out in places like Canada and Japan, the industry will move elsewhere if the local environment is no longer supportive.

Beyond improving health outcomes, the pharmaceutical industry is a key sector of the U.S. economy. In total, pharmaceutical and medicine manufacturing activity helped contribute almost 1.5 million jobs, $147 billion in labor income, $355 billion in value added, and $655 billion in economic output.

The interconnectedness between pharmaceutical manufacturing and R&D is vital, enabling companies to navigate a landscape that demands both ingenuity and economic viability. It is imperative stakeholders and policymakers recognize the crucial importance of sustaining the industry's positive momentum and take proactive measures to mitigate future risks.

The industry's ability to innovate, develop new drugs, and enhance existing treatments relies heavily on substantial and sustained R&D funding. Any disruption or reduction in funding can curtail progress, slow breakthrough discoveries, and hinder the development of life-saving medications. It is vital to prioritize and safeguard the resources necessary for R&D investments, ensuring the industry remains at the forefront of scientific advancement.

A balanced regulatory framework that priorities patients without stifling the industry's capacity for exploration is crucial. Excessive regulations or stringent pricing policies can deter investment, hamper research initiatives, and hinder the industry's ability to deliver affordable and effective healthcare solutions to the public. Striking the right balance between regulation and innovation is essential for sustained progress.

The industry's ability to continue driving advancements in healthcare, contributing to economic growth, and ultimately improving the well-being of individuals relies on the proactive measures taken today to mitigate risks and ensure a robust and resilient future for pharmaceutical manufacturing.

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Appendices

APPENDIX A. DETAILED INDUSTRY DESCRIPTIONS

NAICS 32541 - Pharmaceutical and Medicine Manufacturing

- https://www.census.gov/naics/?input=32541&year=2017&details=32541
- "This industry comprises establishments primarily engaged in one or more of the following: (1) manufacturing biological and medicinal products; (2) processing (i.e., grading, grinding, and milling) botanical drugs and herbs; (3) isolating active medicinal principals from botanical drugs and herbs; and (4) manufacturing pharmaceutical products intended for internal and external consumption in such forms as ampoules, tablets, capsules, vials, ointments, powders, solutions, and suspensions."

NAICS 325411 - Medicinal and Botanical Manufacturing

- https://www.census.gov/naics/?input=32541&year=2017&details=325411
- "This U.S. industry comprises establishments primarily engaged in (1) manufacturing uncompounded medicinal chemicals and their derivatives (i.e., generally for use by pharmaceutical preparation manufacturers) and/or (2) grading, grinding, and milling uncompounded botanicals."

NAICS 325412 - Pharmaceutical Preparation Manufacturing

- https://www.census.gov/naics/?input=32541&year=2017&details=325412
- "This U.S. industry comprises establishments primarily engaged in manufacturing in-vivo diagnostic substances and pharmaceutical preparations (except biological) intended for internal and external consumption in dose forms, such as ampoules, tablets, capsules, vials, ointments, powders, solutions, and suspensions."

NAICS 325413 - In-Vitro Diagnostic Substance Manufacturing

- https://www.census.gov/naics/?input=32541&year=2017&details=325413
- "This U.S. industry comprises establishments primarily engaged in manufacturing in-vitro (i.e., not taken internally) diagnostic substances, such as chemical, biological, or radioactive substances. The substances are used for diagnostic tests that are performed in test tubes, petri dishes, machines, and other diagnostic test-type devices."

NAICS 325414 - Biological Product (Except Diagnostic) Manufacturing

- https://www.census.gov/naics/?input=32541&year=2017&details=325414
- "This U.S. industry comprises establishments primarily engaged in manufacturing vaccines, toxoids, blood fractions, and culture media of plant or animal origin (except diagnostic)."

APPENDIX B. ESTIMATED 2022 IMPACTS

This section uses Census M3 (Manufacturers' Shipments, Inventories, and Orders) data to provide an approximate estimate of impacts attributed to the pharmaceutical and medicine manufacturing industry in 2022. Table B-1 is a copy of Table 3 for comparison.

TABLE B-1. PHARMACEUTICAL AND MEDICINE MANUFACTURING (NAICS 3254) TOTAL IMPACTS, 2021

Unit Indicated

	Employment (1,000 Persons)	Labor Income (Billion $)	Value Added (Billion $)	Output (Billion $)
Direct	291.0	53.7	192.0	354.3
Indirect	495.6	48.0	82.5	160.4
Induced	703.7	45.6	79.9	140.5
Total	1,490.3	147.3	354.5	655.2

TABLE B-2. PHARMACEUTICAL AND MEDICINE MANUFACTURING (NAICS 3254) TOTAL IMPACTS, 2022 (ESTIMATED)

Unit Indicated

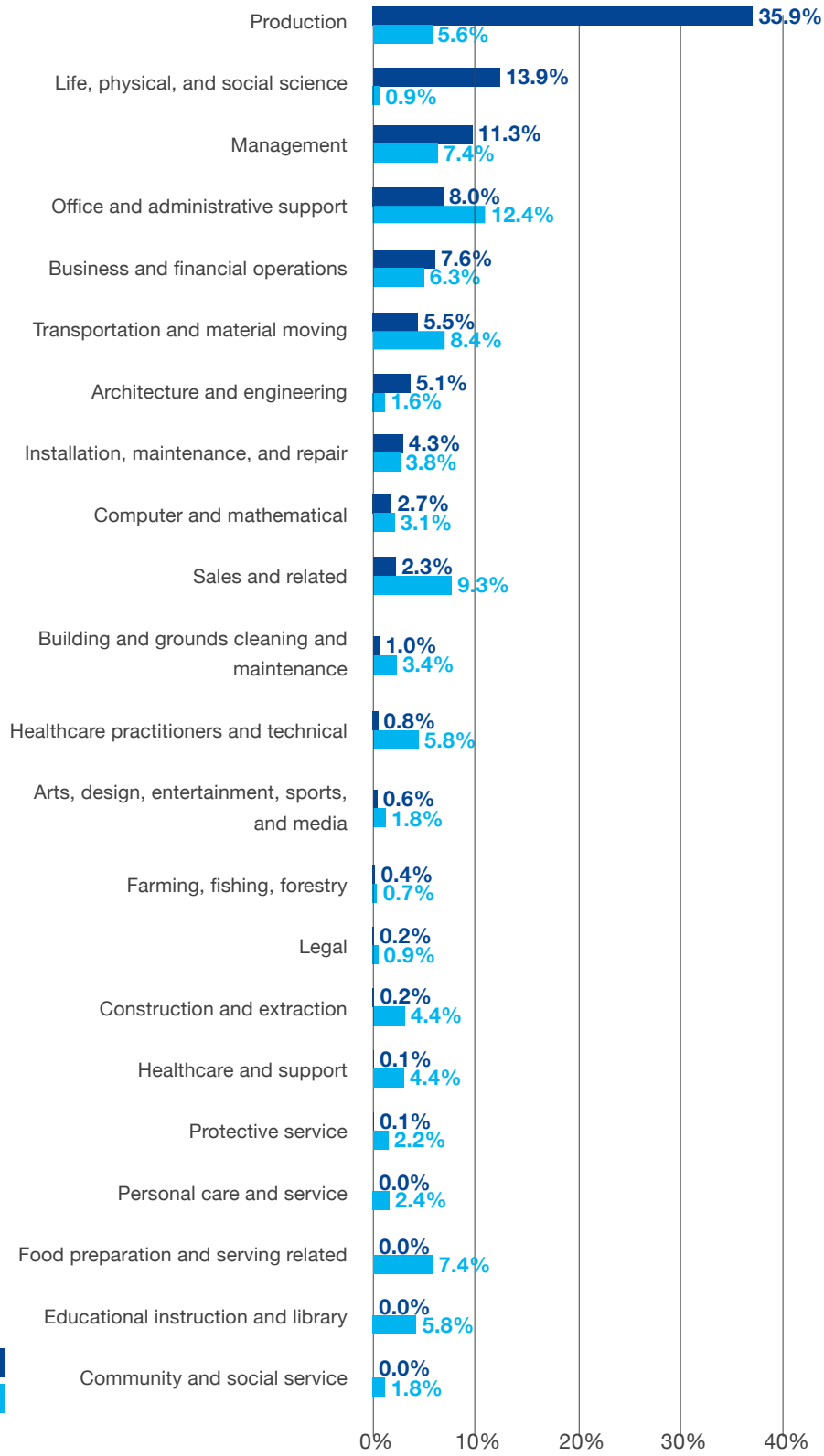
This shows impacts that have been inflated using the growth rate of shipments of pharmaceutical and medicine manufacturing products between 2021 and 2022. These impacts are not based on historical data. Instead, these rough estimates assume that all upstream supply chain and consumption patterns are identical between 2021 and 2022. Additionally, it does not take into account other important factors such as productivity growth.

	Employment (1,000 Persons)	Labor Income (Billion $)	Value Added (Billion $)	Output (Billion $)
Direct	391.8	59.0	211.0	389.4
Indirect	544.6	52.8	90.7	176.3
Induced	773.3	50.1	87.8	154.4
Total	1,637.8	161.9	389.5	720.1

APPENDIX C. OCCUPATIONAL BREAKDOWN

Figure C-1 compares occupations for pharmaceutical and medicine manufacturing (NAICS 3254) versus overall U.S. employment in 2021. Pharmaceutical and medicine manufacturing is represented by significant numbers of the following occupation categories: Production; Life, physical, and social science; Management; Business and financial operations; Architectural and engineering; Installation, maintenance, and repair; and Computer and mathematical.

TABLE C-1. OCCUPATIONAL BREAKDOWN



KEY

Pharmaceutical and Medicine Manufacturing

Total U.S. Employment

Source: Bureau of Labor Statistics

NATIONAL ASSOCIATION OF
Manufacturers