Sustaining the Growth and Competitiveness

of U.S. Biopharmaceutical Manufacturing

DECEMBER 2020

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The strength, resiliency, and responsiveness of the U.S. biopharmaceutical manufacturing industry have stood out as bright spots in our national response to the COVID-19 pandemic, both in ensuring continued patient access to medicines and in increasing manufacturing capacity and ramping up production for potential new treatments and vaccines to counter the virus.

The U.S. biopharmaceutical manufacturing industry's robust U.S. footprint coupled with a globally diverse supply chain is helping our nation meet the demands posed by the COVID-19 pandemic, but our global leadership in biopharmaceutical manufacturing cannot be taken for granted.

Key Takeaways

- With a total economic impact of over $1.1 trillion and more than 4 million jobs, the U.S. biopharmaceutical manufacturing industry is an economic powerhouse for the American economy and workers.

- The industry has generated strong gains in economic output and supporting high wage jobs across a range of skills. U.S. biopharmaceutical manufacturing also involves a large geographic footprint of production facilities across the U.S. and ranks as one of the nation's top exporting sectors for intellectual property (IP)-intensive sectors.

- There is a vast supply chain in the U.S. supporting biopharmaceutical manufacturing. For every worker employed in the biopharmaceutical manufacturing industry, another four jobs are generated across a range of other industries.

- More than half of active pharmaceutical ingredients used in medicines consumed in the U.S. are manufactured in the United States, and there is global diversification in sourcing for those produced outside the United States, led by European nations. China provides a mere 6% of APIs for medicines consumed in the U.S., according to a detailed analysis of U.S. trade data by Avalere Health, one of our nation's leading health care business consulting firms.

- The competitive edge for U.S. biopharmaceutical manufacturing is innovation. Beyond leading the world in new drug approvals, U.S. industry has made advances in manufacturing processes that improve efficiencies, result in more green manufacturing, and enable new complex medicines to be produced as needed by patients across the U.S.

- While the U.S. is a global leader in biopharmaceutical innovation and innovations in manufacturing technologies, other nations are replicating key elements of the U.S. approach to innovation and now outpace U.S. growth in innovation capacities, from scholarly activities to industry research and development to patent innovation.

- The U.S. is increasingly at a disadvantage compared to other countries though in terms of access to a robust STEM workforce—the U.S. projects significant shortfalls across manufacturing industries for highly skilled STEM workers at all levels as the U.S. continues to lag behind other countries in terms of STEM rankings and access to highly skilled workers.

- Recognizing the economic benefits of biopharmaceutical manufacturing, other countries have made significant public investments and introduced a range of tax and other incentives to offset the costs related to building and operating new manufacturing facilities to become more globally competitive with the U.S. In addition, the U.S. is at a significant cost disadvantage to many nations in terms of the costs related to labor, energy, access and costs of raw materials, as well as the costs related to compliance.

- The COVID-19 pandemic has highlighted the importance of having public policies that support resiliency and potential expansions in manufacturing as part of pandemic preparedness and to consider policies that ensure sufficient incentives for R&D and manufacturing investments.

- Encouraging innovation and investment in our biomanufacturing capacities through government and industry working together, rather than mandates, is the best way to continue to grow manufacturing in the U.S.

Introduction

> *Pharma and medtech companies have found themselves front and center—supplying (and rapidly scaling up) vitally important medical products to support patients in their time of need, while also attracting widespread attention as the industry sprints to develop new therapeutics and vaccines for COVID-19."*
>
> *McKinsey & Company, COVID-19 Implications for Life Sciences R&D: Recovery and the Next Normal, May 13, 2020*

The COVID-19 pandemic has raised the public awareness of the critical role the U.S. biopharmaceutical manufacturing industry plays in ensuring the health and well-being of our nation. As McKinsey points out: "Pharma and medtech companies have found themselves front and center—supplying (and rapidly scaling up) vitally important medical products to support patients in their time of need, while also attracting widespread attention as the industry sprints to develop new therapeutics and vaccines for COVID-19."[1]

The U.S. innovative biopharmaceutical industry has been able to ensure continued access to medicines through its robust supply chains while working around the clock to increase manufacturing capacity to meet the projected unprecedented needs for eventual COVID-19 vaccines and treatments. Often overlooked is that these contributions to ensuring the health of Americans are a direct reflection of the economic strength of the U.S. biopharmaceutical manufacturing industry on the world stage and its standing as a leading advanced manufacturing industry in driving economic prosperity and providing high-quality jobs across the nation.

Defining the Biopharmaceutical Manufacturing Cluster

A hallmark of the biopharmaceutical industry cluster is its dynamic nature, both of its constituent companies and of the relationships among them. Companies in the industry include: large, vertically integrated biopharmaceutical companies with their own research and manufacturing facilities; small and start-up companies that have not yet had a medicine approved by the Food and Drug Administration; clinical research organizations and other testing and technical support vendors that provide a range of services to support drug discovery and development; contract manufacturing companies and suppliers supporting manufacturing; and distributors who provide logistics support to deliver prescription medicines.

1 *https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/covid-19-implications-for-life-sciences-r-and-d-recovery-and-the-next-normal*

Looking forward, the U.S. biopharmaceutical manufacturing industry can be expected to continue to offer significant economic spillovers to other U.S. industries that are part of its large supply chain. As the U.S. considers preparedness for future pandemics, it is clear there are opportunities to not just increase resiliency in the pharmaceutical supply chain but also to continue to grow high-wage manufacturing jobs across a network of diverse vendors and suppliers.

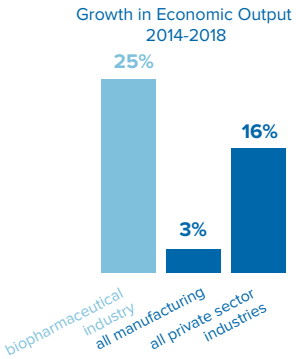
In the ongoing discussions of how to increase the biopharmaceutical manufacturing presence in the U.S. it is imperative to keep in mind the economic importance of this industry, the reality of rising global competition it confronts, and the role of the biopharmaceutical industry in sustaining and growing our economy.

The facts about the larger economic landscape facing the U.S. biopharmaceutical manufacturing industry are presented in this report to inform policymakers and other stakeholders as they consider how best to ensure our biopharmaceutical manufacturing industry cluster remains globally competitive, a driver for U.S. economic prosperity, and well-positioned to serve the health needs of Americans in the future. This information should also inform public policies seeking to increase U.S.-based manufacturing of medicines, highlighting the opportunity created by advanced manufacturing technologies to continue to drive increased U.S. economic prosperity.

Economic Contributions of the U.S Biopharmaceutical Industry

Among the standout contributions of the biopharmaceutical manufacturing industry to the U.S. economy are that it:

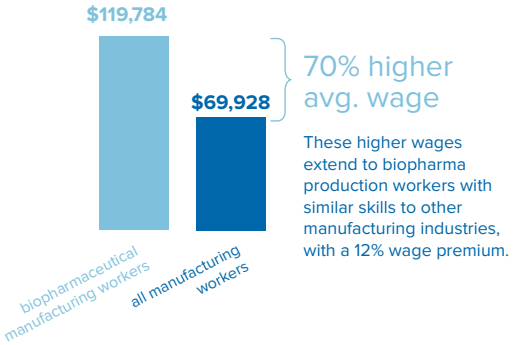
Generates Strong Gains in Economic Output:



Sustains Outsized Levels of Productivity:

Reflects a high level of productivity that stands over three times higher than manufacturing overall.

Supports High Wage Jobs Across a Range of Skills:



70% higher avg. wage

These higher wages extend to biopharma production workers with similar skills to other manufacturing industries, with a 12% wage premium.

Involves a large geographic footprint of production activities across the U.S.

in the US involved in the production of medicines under current Good Manufacturing Practice regulations. These facilities are spread across 45 states, the District of Columbia and Puerto Rico, with 37 states and Puerto Rico having 5 or more such facilities.

Generates a High Level of Exports

$66B
in 2019 and growing by
138%
since 2004.

U.S. exports of pharmaceuticals and medicines stands second only to aerospace among science and technology industries

U.S. Biopharmaceutical Manufacturing is an Economic Powerhouse for the American Economy and Workforce

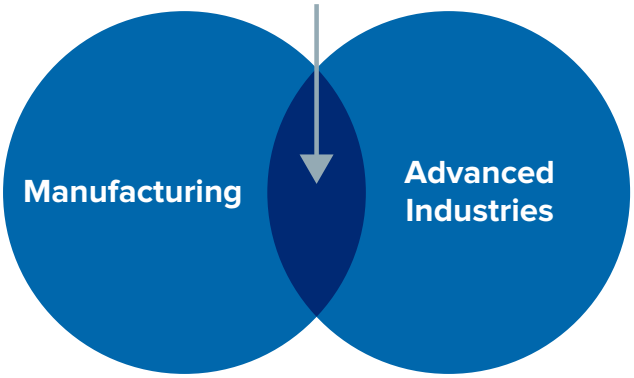
The U.S. biopharmaceutical manufacturing industry is economically powerful because it stands at the intersection of high-value, export-oriented manufacturing and what the Brookings Institution calls the "Advanced Industries" – a sector that requires high levels of science and engineering innovation. Biopharmaceutical manufacturing qualifies as this kind of "innovation-led manufacturing industry" because of its tight linkage to high levels of biomedical R&D and its employment of a disproportionately high share of workers who have been trained in the STEM (science, technology, engineering, and mathematics) fields.

For example, in the broader manufacturing sector, about 10% of jobs require STEM skills. But in biopharmaceutical manufacturing, as many as one-third do. Some of these jobs can be found in the higher-skilled end of the production occupations (e.g., Quality Assurance inspectors), often held by workers with some degree of technical training. Other jobs in research, development, drug design, and process engineering require advanced scientific and engineering education. In broad terms, firms that develop and manufacture biopharmaceuticals offer high-paying jobs precisely because these jobs require such high levels of STEM skills. There are high-wage jobs in this sector at all levels from production operator through senior management.

In many ways, the biopharmaceutical manufacturing industry stands as an ideal economic driver for sustained growth and prosperity in the United States. It grows in output and employment even in tough economic times. It provides high wage, good quality

Innovation-Led Manufacturing Leads the Way

Manufacturing Benefits:
- High quality jobs across a mix of skills
- Significant supply chains that magnify job creation potential as production rises
- Export oriented



Advanced Industries' Benefits:
- Leading industries in innovation
- Deploy science, technology, engineering and math skills
- Most competitive industries in U.S.
- High productivity

For every one worker employed in the biopharmaceutical manufacturing industry another four jobs are generated across a range of other industries.

jobs. It has a large geographic footprint across nearly every state. It drives innovation and deploys technologies that provide a comparative advantage for U.S. companies. It generates a significant level of exports. It has a strong supply chain that drives economic growth across the economy. Yet all these economic benefits are but icing on the cake to the value of the medicines being manufactured to improve the health and quality of life for humankind.

Other closely-related specialized biopharmaceutical industries are core to the functioning of the U.S. biopharmaceutical innovation and manufacturing ecosystem, including contract research organizations involved in preclinical development and clinical trials, start-ups and early stage biopharmaceutical companies focused on commercial research that has not yet generated new medicines, contract manufacturers and other vendors and suppliers filling production gaps, providing redundancy in the supply chain, and a complex biopharmaceutical distribution system.

The bottom line for the U.S. economy is that the biopharmaceutical industry has significant national economic impacts that help drive more than 4 million jobs. As both a manufacturing and advanced industry, U.S. biopharmaceutical manufacturing does not stand alone but is part of a larger innovation complex required to discover, develop, produce, and distribute medicines to patients.

The vast supply chain of other manufacturers and service providers accounts for more than 1.42 million of these jobs. This includes significant purchases by the biopharmaceutical manufacturing industry from other manufacturers from packaging, various ingredients, high-precision measuring and analytic tools, and production automation components. While some have expressed concern that there may be over-reliance on countries that may pose a national security concern for certain pharmaceutical goods, particularly for supplies of active pharmaceutical ingredients (API), the reality is that API facilities reflect substantial global diversity.

In 2019, 54% of the $86.5 billion of API used in medicines consumed in the U.S. were manufactured within the U.S. The largest foreign suppliers, providing 26% of the value of APIs, are found in Europe, led by Ireland which supplies 19% of the value of APIs.

> *"CDER's [the FDA Center for Drug Evaluation and Research] analysis shows that overall, China has only a modest percentage of the facilities able to produce APIs for the U.S. market."*
>
> *Janet Woodcock, M.D., Director – FDA Center for Drug Evaluation and Research*

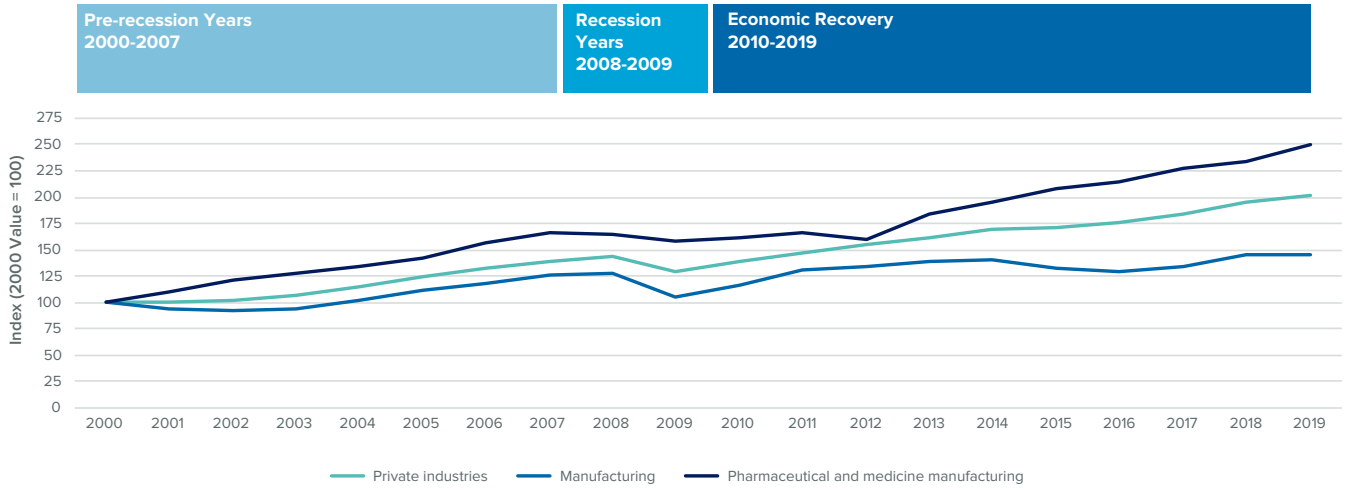
In contrast, China provides a mere 6%.[2] Plus, the FDA's own data determined that there are only three medicines on the World Health Organization's Essential Medicines list whose API manufacturers are solely based in China.[3]

Another **1.81 million jobs** are generated across the U.S. economy through the high wages paid to biopharmaceutical workers that lead to personal spending on goods and services for an even broader range of industries in the U.S.

As we look towards sustaining the U.S. economy in the recovery from COVID-19, the biopharmaceutical manufacturing industry can be expected to lead the way. The continued demand for medicines and vaccines through challenging as well as good economic times has historically meant that the biopharmaceutical sector can help ease downturns and propel future growth. This can be seen over the period of 2000 to 2018 when biopharmaceutical manufacturing was a leader during times of economic growth, and provided a cushion during economic downturns, as during the Great Recession of 2008-2009.

Figure 1. Biopharmaceutical Industry Leads Economic Growth at All Stages of the Business Cycle from 2000-2019:

Comparison of Economic Output of Biopharmaceutical Manufacturing to All Private Sector Industries and All Manufacturing Industries



Source: *U.S. Bureau of Economic Analysis*

2 *Avalere, "Majority of API in US Consumed Medicines is Produced in the United States," July 15, 2020*

3 *"Safeguarding Pharmaceutical Supply Chains in a Global Economy", Testimony of Janet Woodcock, M.D., Director – Center for Drug Evaluation and Research, U.S. Food and Drug Administration before the U.S. House Committee on Energy and Commerce, Subcommittee on Health, October 30, 2019. https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019*

Innovation Stands as the Competitive Edge for the U.S. Biopharmaceutical Manufacturing

Innovation is at the heart of what makes the U.S. biopharmaceutical manufacturing industry stand out as a world leader, and why it is able to generate such a high health dividend to Americans.

Innovation and manufacturing fit together in a tightly bound partnership. In the first place, biopharmaceutical R&D – whether in large corporations, university laboratories, or small startups – is often the starting point for the development of new treatments and potential cures. As the scientific complexities involved in medical research have increased so have the manufacturing processes with a growing need for new technologies and specialized manufacturing facilities. These manufacturing facilities have a sustainable economic future exactly because they use the latest advanced technologies to achieve high levels of efficiency and productivity. Moreover, as has been demonstrated by researchers at the Harvard Business School, domestically based manufacturing often leads to the next generation of innovative products, by involving researchers in the challenges of production.[4] Conversely, the Harvard researchers argued, if an innovation-intensive manufacturing sector moves overseas, the underlying R&D may inevitably migrate to follow them offshore. Maintaining the U.S. lead in biopharmaceutical R&D requires enabling the simultaneous leadership in pharmaceutical manufacturing.

Today, the U.S. stands first in the world in biopharmaceutical innovation, as shown in terms of its leadership in peer-reviewed publications, industry research and development, intellectual property generation and venture capital investments. Even among U.S. advanced industries, the biopharmaceutical manufacturing industry stands out. In its ground-breaking study of advanced industries, The Brookings Institution found that the biopharmaceutical manufacturing industry leads with the highest R&D spending per worker at $143,110, well ahead of the second place communications equipment industry, at $91,428 per worker.[5]

Another clear sign of the innovation strength of the U.S. biopharmaceutical manufacturing industry is that it leads the world in the development of new medicines. Nearly half of all new medicines approved for patients over the past five years have been developed by biopharmaceutical companies headquartered in the U.S.[6] With 125 new drugs developed by U.S. biopharmaceutical companies from 2014-2018, the U.S. stands at twice the level of Europe and nearly 4 times the level of Japan.[7]

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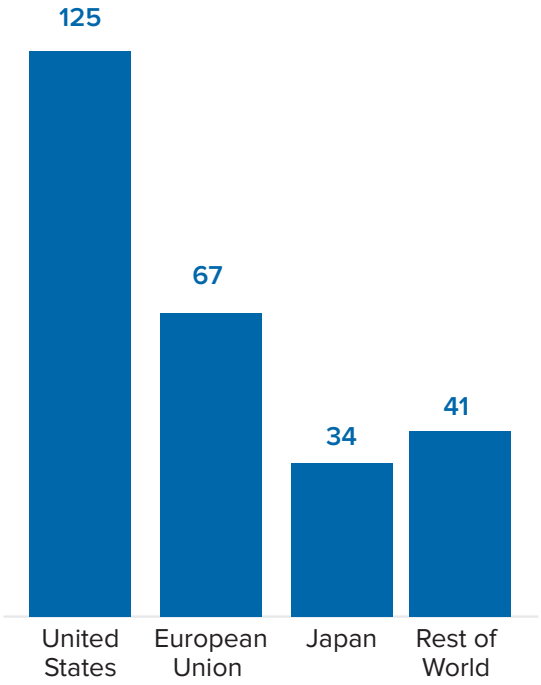
4 *See work of Pisano and Shih, Producing Prosperity: Why America Needs a Manufacturing Renaissance, Harvard Review Press, 2012.*
5 *Brookings Institution, America's Advanced Industries: What They Are, Where They Are, And Why They Matter, Brookings Advanced Industries Project, February 2015, page 11.*
6 *While most large biopharmaceutical companies are multinational, the location of company headquarters is indicative of where companies' activities are centered and where their intellectual property is located.*
7 *European Federation of Pharmaceutical Industries and associations, The Pharmaceutical Industry in Figures: Key Data, 2019*

Figure 2. New Chemical and Biological Entities Developed From 2014-2018 by Location of Biopharmaceutical Company Headquarters



The U.S. pipeline of new medicines in development is also quite extensive. As of 2019, there were approximately 4,500 new medicines in development in the U.S. for a wide range of diseases.[8] An average of 74% of new medicines in development are first-in-class medicines demonstrating the important role that the biopharmaceutical industry cluster plays in advancing major breakthroughs taking place in biomedical research.[9]

It is also important to note that many of the novel medicines recently developed are actually produced here as well. These novel medicines are often among the top selling medicines in the U.S. given that they are meeting previously unmet medical needs including treatments for autoimmune disease, diabetes, Hepatitis C, epilepsy, and cancer. Using the NIH Daily Med and Drugs@FDA databases that identifies the manufacturing locations of individual

Benefits of Medical Innovation to U.S. Patients

The ultimate value of the U.S. innovation-led biomanufacturing industry is the high levels of economic gains from improved health and longevity for patients. There have been tangible economic benefits from advances in medical innovations reaching patients. Health economists have estimated that for the U.S., our declining mortality rates from 1970 to 2000 (an increase of 6 years in life expectancy) had a value to society of more than $3 trillion a year, equal to about half of the average annual gross domestic product (GDP) over that period.*

Additionally, a key benefit of having the U.S. lead in development of new medicines is that U.S. patients often have better, more rapid access to these novel therapies, which strongly influences their development to meet the unique needs of U.S. patients. Patients in other developed countries have access to cancer medicines, on average, at least two years later than U.S. patients.**These delays have important implications for patient outcomes. If U.S. patients diagnosed with the most common form of lung cancer had the lower levels of access experienced in other wealthy countries, aggregate survival gains from 2006 to 2017 would have been cut in half.***

** Kevin M. Murphy and Robert H. Topol, "The Value of Health and Longevity," NBER Working Paper No. W11405, June 2005.*

*** IMS Consulting Group report for PhRMA. Patient access to innovative oncology medicines across developed markets. June 2016.*

***PhRMA analysis of IQVIA Analytics Link and FDA, EMA, PMDA, TGA and Health Canada data. May 2019.*

**** HIS Markit. Comparing Health Outcome Differences Due to Drug Access: A Model in Non-Small Cell Lung **Can**cer. December 2018*

8 *Adis R&D Insight Database, April 2019*

9 *Long G; Analysis Group. The biopharmaceutical pipeline: innovative therapies in clinical development. http://phrma-docs.phrma.org/files/dmfile/Biopharmaceutical-Pipeline-Full-Report.pdf. Published July 2017.*

> *In the world of discovering and developing medicines, chemistry and biology are at the heart of manufacturing. Manufacturing advances in the biopharmaceutical industry contribute increasingly sophisticated enhancements to these fundamental processes. Research that yields a promising new molecule, for example, may require new applications of chemistry or biology to synthesize the molecule, and new or improved facilities and equipment to transform living material into a medicine."*
>
> *Deloitte, Advanced Biopharmaceutical Manufacturing: An Evolution Underway, 2015*

medicines, an analysis of the top 20 medicines sold in the U.S. in 2017 found that more than 83% are manufactured in the U.S. This reflects the first mover status of the U.S. due to the global leadership of U.S.[10] biopharmaceutical manufacturing companies in the discovery and development of novel medicines.

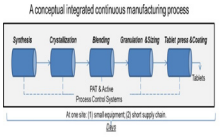
The innovation taking place by the biopharmaceutical manufacturing industry reaches far beyond researching and developing new medicines. The innovation also involves and encompasses advances in the manufacturing processes to scale-up production of novel drugs from immunotherapies to gene therapies to regenerative medicines. Biopharmaceutical manufacturers are constantly innovating and adopting new technologies to keep pace with scientific advances made through R&D, to advance R&D capabilities, and to obtain efficiencies and potentially cost savings in the manufacturing process. Without this continued focus on innovation, manufacturers would not be able to produce the complex yet impactful new medicines of today.

The critical need for manufacturing innovations (see text box) for novel medicines means that advances in biopharmaceutical manufacturing serve as an essential link between the discovery of a medicine and its availability to patients. These advances in manufacturing innovations are critical for driving future competitiveness of U.S. biopharma manufacturing especially in light of lower cost places to doing high value manufacturing. and overcoming the high-input-cost environment.

And these advances in manufacturing processes must meet a very high standard. To a degree unmatched by other manufacturing industries, all biopharmaceutical manufacturing is conducted under especially high standards, with strict requirements and rigorous approvals and inspections by the U.S. Food and Drug Administration to ensure the safety, quality and reliability of medicines to protect patients and deliver the intended therapeutic benefits.

10 *An analysis conducted by NDP for PhRMA based on U.S. sales from Top spending by drug: Medicines Use and Spending in the U.S. – A Review of 2017 and Outlook to 2022, IMS Institute for Healthcare Informatics, April 2018; Manufacturer locations from NIH Daily Med and Drugs@FDA database*

Examples of manufacturing process innovations being advanced by the biopharmaceutical industry include:



CONTINUOUS MANUFACTURING

Challenge: Produce greater quantities of medicines on demand more quickly is a key challenge.

Solution: Instead of manufacturing in batches, continuous manufacturing involves a fully integrated process in the production of medicines that avoids the need to order and install new equipment to adjust changes in demand, eliminates wasteful downtime for emptying/cleaning/refilling batch reactors, and improves the ability to carry out ongoing quality monitoring.. While this is not the solution for all medicines, it can provide efficiencies where appropriate.

SINGLE-USE SYSTEMS

Challenge: Biopharmaceutical manufacturing facilities producing large molecule medicines require significant time and investment in specialized equipment, such as sterilizing apparatus, bioreactor systems and process analytic technologies. Depending on the size of the facility, manufacturers may have limited ability to manufacture multiple products at one facility given the substantial complexity, time and investments required.

Solution: Involves use of disposable components replaced after each use in the manufacturing process. A key advantage of single-use systems is flexibility in using the same floor space to manufacture different types of low volume products, reduced production lead times, and lower capital investment and reduced water and energy requirements for washing and sterilization.

HIGH-VOLUME CELL PROCESSING ADVANCES

Challenge: Current methods of cell processing are not keeping up with the development of new cell-based medical products that introduce living cells to replace or repair damaged or diseased cells, such as in acute diseases such as stroke or spinal cord injury. One of the biggest challenges is ensuring the potency, consistency, and safety of the cells at an economically viable cost.

Solution: To support the manufacture of a variety of new cell-based medicines, next-generation cell expansion technologies are being advanced to enable high- volume cell processing, such as automated closed bioreactor systems, bioreactors with parallel processing capabilities and novel high-yield culture media alternatives to optimize cellular productivity.

ADVANCED PURIFICATION TECHNOLOGIES

Challenge: A critical component of large molecule manufacturing is purification. Purifying the product removes “junk” and potentially harmful materials ensuring that only the target molecule is collected at the end of the manufacturing process. The purification process is extremely complex, resource intensive, and time consuming.

Solution: New innovative chromatography tools and resins, chromatography-free purification methods, and new technologies for purification of biological fluids using high permeability membranes are designed to remove processing bottlenecks and introduce numerous efficiencies throughout the manufacturing process, result in greater yields and speeding up production.

CELL PRESERVATION, DISTRIBUTION AND HANDLING METHODS

Challenge: For certain cell-dependent products such as biologics and gene- and cell-based therapies, manufacturers are faced with the challenge of maintaining products in transit at specific temperature ranges, as well as developing more cost-effective preservation methods that are able to ensure cell stability at high volume and over long periods of time. In some cases, costs of cell product distribution can be higher than the manufacturing costs.

Solutions: A range of approaches are being explored to increase efficiencies, including advanced cryopreservation technologies, alternative preservation technologies for cell types, such as skin cells, that do not maintain potency after being frozen, complex product tracking systems, and enhanced cell bank storage infrastructure.

Still, U.S. Biopharmaceutical Manufacturing Facing Headwinds from International Competition

Today, the U.S. biopharmaceutical manufacturing industry is a world leader. But the rest of the world is catching up, and quickly! The trends are clear that a more intensive and globalized competition for the biopharmaceutical industry is taking root, with many nations in the developing world joining European competitors in seeking to challenge U.S. global leadership in innovation.

An examination of the top 18 nations in biopharmaceutical cluster development, including China, South Korea, Singapore and nations from across the European Union, finds that the U.S., while still leading in many innovation measures, has been growing much more slowly than its competitors. With comparative growth rates in key innovation metrics like those shown below, it requires little imagination to see that the U.S. risks falling behind in nearly every measure of biopharmaceutical innovation.

The one measure on which the U.S. has outpaced the average growth of the top 18 nations is biopharmaceutical value-added. This is significant and demonstrates the strength of U.S. biopharmaceutical manufacturing on the world stage because value-added considers the economic contribution of manufacturers beyond the supplier goods purchased to produce a finished product.

The overall situation of generally lagging growth in biopharmaceutical innovation for the United States is found in the following statistics:

- In peer-reviewed biopharmaceutical-related publications, the U.S. only grew by 9.6% from 2014-2019, while the comparison nations' average grew by 25.3%. The U.S. now comprises slightly more than one-third of publications activity across the nations examined.

China Targeting Biopharmaceutical Industry for Development

> *"The State Council executive meeting decided to innovate and upgrade the pharmaceutical industry, an industry not only crucial to public health, but also to the development of an innovative economy ... Pharmaceutical industry requires tremendous investment in early stages, but pays off in the long run. In the economic "new normal,", pharmaceutical enterprises should not only stick to research and development, but also focus on talent training as well as the transformation of research results into industrial products."*
>
> *People's Republic of China, State Council Statement of Feb. 15, 2016*

- In biopharmaceutical industry-funded research, the U.S. remains dominant with nearly two-thirds of industry research activity, but the U.S. healthy gain of 16.9% from 2014-2017 lagged the comparison nations' average growth of 26.8%.

- In biopharmaceutical-related patent growth, the U.S. grew 13.4% from 2014-2019, compared to the 19.0% average across the benchmark nations, and now only stands at slightly more than one-third of total patent innovation taking place among these nations.

- In biopharmaceutical-related venture capital investment, the U.S. remains dominant, capturing just over two-thirds of industry investment activity among the benchmark nations. However, the benchmark nations are gaining a foothold with an average growth rate of 245% from 2014-2019 —double the U.S. growth of 121%.

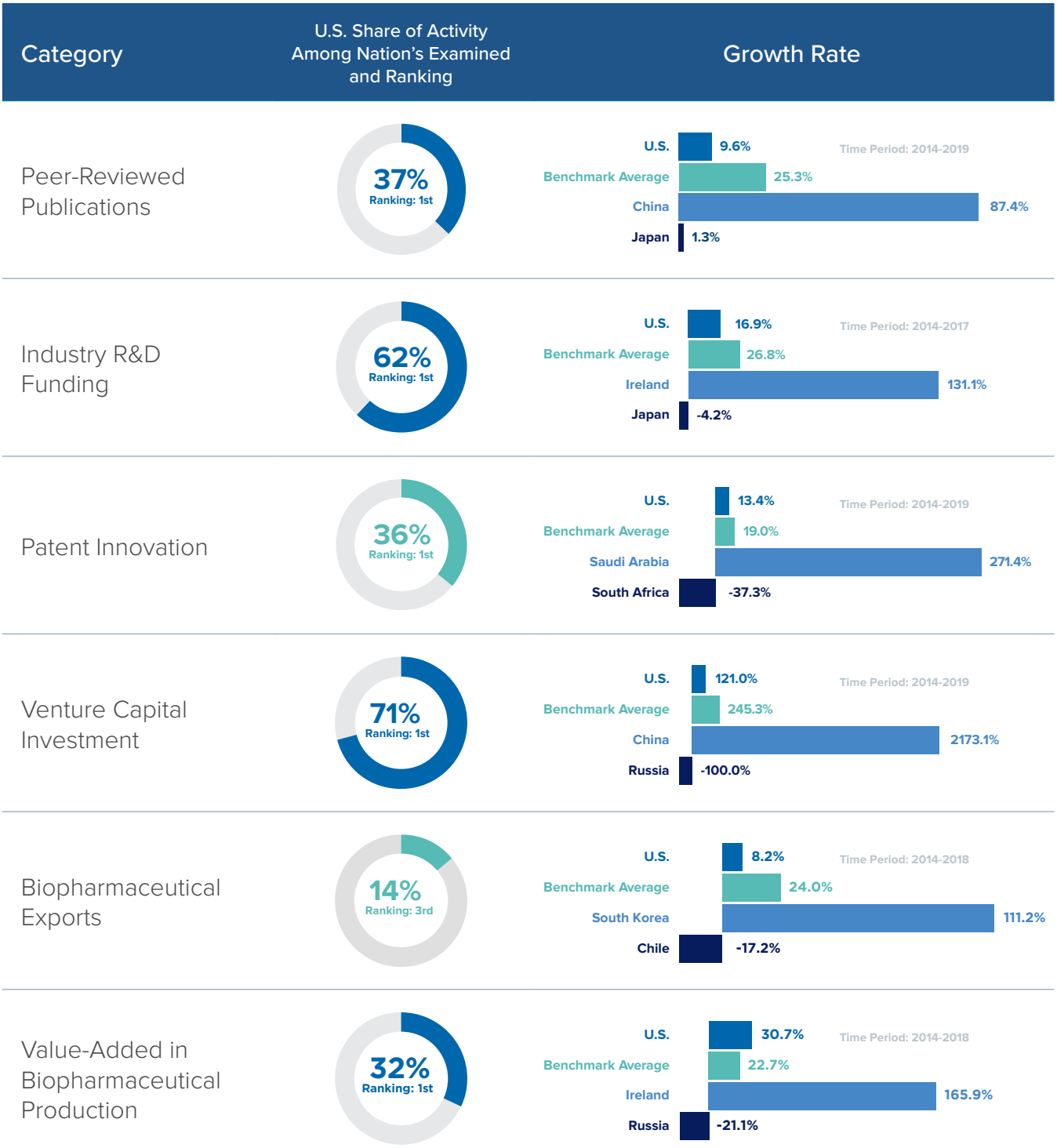
- In biopharmaceutical exports, the U.S. ranks 3rd among the top 18 nations, with a market share of 14% among top nations, but its growth is lagging over the 2014-2018 period with an 8.2% gain for the U.S. compared to 24% for the top 18 nations.

Benchmarks:
Leading Comparison Nations

- Australia
- Brazil
- Canada
- Chile
- China
- France
- Germany
- Ireland
- Israel
- Italy
- Japan
- Russia
- Saudi Arabia
- Singapore
- South Africa
- South Korea
- Sweden
- United Kingdom

- In biopharmaceutical value added, the U.S. ranks 1st among the comparison nations accounting for a third of the biopharmaceutical value added of the nations examined. The U.S. industry's growth in value added from 2014-2018 of 30.7% exceeds the average of the 18 benchmark nations' growth of 22.7% but does lag key emerging competitors such as Ireland at 165.9% and China at 70.9%.

Figure 3. Benchmark Nations Closing the Gap on U.S. Leadership

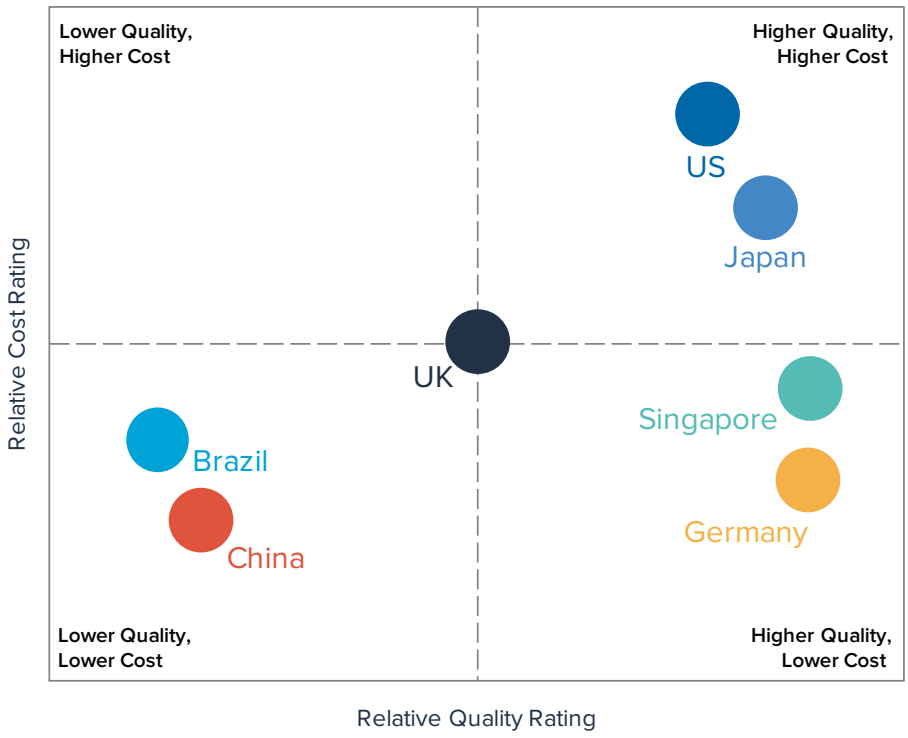


Sources: *i. Peer-Reviewed Publications: Clarivate Analytics' Web of Science; key fields analysis by TEConomy Partners; ii. Industry R&D Funding: OECD Main Sci¬ence and Technology Indicators Database. Comparable data over the period available only for Canada, China, France, Germany, Ireland, Israel, Italy, Japan, Singapore, South Korea, Sweden, and the United Kingdom. iii. Patent Innovation: WIPO statistics database. Last updated: April 2020; iv. Venture Capital Investment: PitchBook venture capital analysis database; v. Biopharmaceutical Exports: OECD Main Sci¬ence and Technology Indicators Database; vi. Value-Added in Biopharmaceutical Production: National Science Board, Science and Engineering Indicators 2020, Supplemental Table S6-6.*

In head-to-head comparisons of the United States to key competitors as a potential site for investments in expanded and new manufacturing, the U.S. is viewed as a high value location but a high cost one. The figure below is from a 2014 analysis conducted by Battelle which surveyed senior-level strategic planning executives from biopharmaceutical companies involved in making real-world decisions about where to locate biopharmaceutical operations. Executives were asked to rate regions on quality and cost attributes associated with locating investments in the U.S. and key competitor nations, and were of the view that the U.S., although a high-quality manufacturing region, was also the most costly.[11]

The high cost environment found in the U.S. compared to other countries is confirmed by The Conference Board and its International Labor Comparisons program. It finds that in hourly compensation costs the U.S. ranks among the highest in the world at $39.03 per hour in 2016, while India and China stand less than $5 per hour.[12] Overall, producing API in China and India results in an estimated 30-40% cost reduction for manufacturers, due to labor cost advantages.[13] Additionally, there are often substantial differentials in the cost of raw materials and energy-related inputs between the U.S. and other countries, as well as lower environmental regulation. China, for example, has lower electricity, coal, and water costs than the U.S. and also faces fewer environmental

Figure 4. Rating by Senior Level Biopharmaceutical Strategic Planning Executives of Quality and Cost Attributes for Locating a Biopharmaceutical Manufacturing Facility in the U.S. and Key Competitor Nations



11 *Battelle, The U.S. Biopharmaceutical Industry: Perspectives on Future Growth and The Factors That Will Drive It, commissioned by PhRMA, 2014.*

12 *The Conference Board, "International Comparisons of Hourly Compensation Costs in Manufacturing, 2016 - Summary Tables." Note that for China and India data on manufacturing hourly compensation was reported only through 2013 and stood at slightly more than $4 per hour for China and roughly $1.50 in India, with significant data limitations.*

13 *FDA's 2011 report, "Pathway to Global Product Safety and Quality."*

regulations regarding buying, handling and disposing of toxic chemicals, leading to lower direct costs.[14]

Additionally, other countries recognize the economic contributions of this industry and work hard to attract biopharmaceutical R&D and manufacturers through various tax and other incentives. In terms of tax supports for research and development, the U.S. currently ranks 24th place among OECD and BRIC countries.[15]

Fortunately, the Battelle study on perspectives of senior-level strategic planning executives also examined views on projected growth rates and found that efforts to make reasonable improvements in the cost structure of the U.S., while sustaining high quality standards, could make a significant difference, perhaps increasing biopharmaceutical manufacturing by more than 30% over a 10-year period. For example, calls for expediting and streamlining regulatory processes could have positive effects for increasing domestic manufacturing. This suggests the U.S. can maintain its competitive edge and remain a global leader in biopharmaceutical innovation with a constructive, pro-active policy approach that embrace both regulatory streamlining along with manufacturing innovations to offset the higher U.S. cost environment.

14 *https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019*
15 *https://itif.org/publications/2020/09/08/enhanced-tax-incentives-rd-would-make-americans-richer*

U.S. Biopharmaceutical Manufacturing Requires Proactive Policies to Spur its Competitive Position

> Prior to 1980, European firms defined the industry, both in terms of market presence and in their ability to create and produce innovative new products .... But beginning in the 1980s, the United States surged to the forefront of biomedical innovation. This sudden and remarkable shift was no accident: It was the result of strong policy positions taken by the federal government.
>
> **Milken Institute, The Global Biomedical Industry: Preserving U.S. Leadership**

The COVID-19 pandemic has elevated the economic and health imperative for the U.S. to remain a global leader in biopharmaceutical manufacturing. Over the past 30 years, the United States earned its global leadership in the advanced manufacturing cluster of biopharmaceutical manufacturing by focusing on policies and capabilities to translate innovations into novel treatments to address unmet patient needs. The hallmarks of our biopharmaceutical innovation ecosystem include:[16]

- Sustained public investment in basic medical research
- Enlightened public policies supporting technology transfer and IP protection
- Sustained venture financing, especially at early stages of firm development
- A robust market for new treatments and technologies

Maintaining these policies and exploring whether additional policies to support key infrastructure investments and to help ensure a level playing field with the incentives being offered by other countries will be critical to sustaining and growing biopharmaceutical manufacturing in the U.S. In order for the U.S. to keep pace with the intense global competition for biopharmaceutical manufacturing, it must shore up key aspects of its overall innovation ecosystem.

Similarly to U.S. competitors, who are viewing the COVID-19 pandemic as an opportunity for doubling down on their investments across the overall biopharmaceutical innovation ecosystem, the U.S. must do the same – focusing on areas that are posing barriers to growth, including:

- Create Incentives for Innovations and Investments in New Technologies and Technology Platforms including Advance Manufacturing and Green Manufacturing Technologies

16 *For fuller explanation of the development and rise of the U.S. biopharmaceutical industry see: Landau, Achilladelis and Scriabine, Pharmaceutical Innovation: Revolutionizing Human Health, Chemical Heritage Foundation, 1999 and Daemmrich and Bowden, Rising Drug Industry, Chemical & Engineering News, June 20, 2005, Volume 83, Number 25; DeVol et. al., The Global Biomedical Industry: Preserving U.S. Leadership, Milken Institute, September 2011*

- Promote and Deepen Public-Private Collaborations
- Make Critical Investments to Address Shortfalls in STEM Talent

Create Incentives for Biopharmaceutical Manufacturing Investment and Innovation:

The cost in both time and resources of bringing on-line biomanufacturing facilities can be a significant barrier to accelerating biopharmaceutical industry growth. Average costs of building a new manufacturing facility can reach above hundreds of millions of dollars. It is not unheard of for individual biopharmaceutical companies to make investments of multiple billions of dollars to address needs for highly specialized, large-scale production facilities for complex biologics, such as a $2 billion investment in new production facilities for diabetes treatments announced in 2015.[17] Building such capacity and obtaining regulatory approval to produce a medicine can take four to five years, and it could be as many as ten years before a complex manufacturing supply chain for a medicine reaches its global peak, reflecting the need to comply with the regulatory standards of the countries where a medicine is sold. Similarly, expanding or enhancing existing facilities and transferring a single product to a new manufacturing site can take several years given the need for technology transfer, scale-up, validation, stability protocols, and regulatory filings.[18]

Numerous international competitors are promoting incentives for investments in biopharmaceutical manufacturing, which has only accelerated in light of the COVID-19 pandemic. Notable efforts include:

- India's $1.3 billion "Production Linked Incentive Scheme" that offers pharmaceutical manufacturers partial rebates tied directly to their investment in greenfield production capacity. In broader public sector investments, India through its National Biotechnology Strategy 2015-2020[19] is promoting bioscience research, education and in the overall context of the Modi government's "Make it India" policy agenda. This includes support for supporting research infrastructure to support biomanufacturing and advancing incubators and technology parks across India through the Department of Biotechnology.[20]

- Singapore's offer of super-deductions for R&D and preferred tax treatment of manufacturing based on IP created locally, known as an IP Development Incentive. Plus, there is a 100% deduction from corporate income taxes for investments in advanced manufacturing equipment.[21]

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17 *Novo Nordisk Plans $2 billion Investment in New Production Facilities in US and Denmark, Manufacturing Chemist, August 26, 2015*
18 *Otta et. al., Rapid Growth in Biopharma: Challenges and Opportunity, McKinsey & Company, December 1, 2014*
19 *http://dbtindia.gov.in/sites/default/files/DBT_Book-_29-december_2015.pdf.*
20 *http://dbtindia.gov.in/schemes-programmes/translational-industrial-development-programmes/biotech-parks-incubators and http://dbtindia.gov.in/sites/default/files/DBT_Report_R2V6_250219%20%281%29.pdf*
21 *https://www.edb.gov.sg/content/dam/edbsite/how-we-help/incentives-&-schemes/IDI%20circular%20(Jan2020).pdf.*

> *The opportunities offered by the pharmaceutical and biotech industry strengthen a region's workforce development program by creating the construction jobs that represent the backbone of long-standing, well-regarded apprenticeship programs. In doing so, the industry is intrinsically supporting one of the few remaining pathways to the middle-class for millions of non-college educated men and women across the country: the skilled construction trades."*
>
> *Institute for Construction Economic Research, 2018*

- Russia's regular negotiation of "specialized investment contracts" that incentivize domestic and inward investments in pharmaceutical manufacturing capacity through partial reimbursement of drug-development costs and clinical trials and other concessions.[22]

- Japan's COVID-19 stimulus package, which includes funding for up to half the investment required for new domestic manufacturing sites. For products and materials on which Japan is highly reliant, the government will cover up to two-thirds of the necessary investment.[23]

- For China, the biopharmaceutical industry is one of targeted sectors set out in the "Made in China 2025" program, designed to move domestic producers up the value chain and better integrate manufacturing with innovation to China can meet its own needs while also competing in export markets. "Made in China 2025" functions by offering tax preferences to encourage firms to shift both production and R&D to China, and also offers various other direct subsidies for R&D, overseas acquisitions, and talent recruitment.[24]

Advancing a package of incentives to support increased biopharmaceutical manufacturing investments could help address the high cost location disadvantage of operating in the U.S., while also encouraging the advancement of innovations in green manufacturing, enabling efficiencies that allow U.S. producers to compete with countries with less-stringent environmental regulations. Plus, investments in biopharmaceutucal manufacturing infrastructure translates into significant gains in construction jobs. A detailed study of the investments made in biopharmaceutical plants across 11 states from 2012-2017 found more than $22.4 billion invested, which in turn generated a demand for 23,000 construction jobs with the highest demand being for skilled electricians, instrumentation techs, plumbers, carpenters and millwrights.[25]

The response by U.S. biopharmaceutical companies to recent corporate tax reform suggests that incentives for production in the U.S. do work. Public announcements by biopharmaceutical companies following corporate tax reform amounted to more than $27 billion in new investment in research and manufacturing facilities.[26] Deloitte Insights reported in its survey of biopharmaceutical executives that a majority intended to invest in R&D, general business operations and capital projects.[27]

Even with recent corporate tax reform, however, the U.S. finds itself with less robust tax and other incentives compared to other nations, who are active players in the biopharmaceutical manufacturing network. For instance, Ireland, which generates 19% of the value of active pharmaceutical ingredients (APIs) consumed in the U.S.[28], continues to offer a low corporate tax

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22 *https://minpromtorg.gov.ru/common/upload/files/docs/Instruments_of_government_support_for_localization_of_foreign_productionin_Russia_V.S._Osmakov.pdf.*
23 *Office of the Prime Minister of Japan, "On the Emergency Economic Measures in Response to the New Corona Virus," April 7, 2020. See https://www5.cao.go.jp/keizai1/keizaitaisaku/2020/20200407_taisaku.pdf*
24 *Congressional Research Service, "Made in China 2025" Industrial Policies: Issues for Congress, August 11, 2020, see https://fas.org/sgp/crs/row/IF10964.pdf.*
25 *Russell Ormistron, Research Scholar, Institute for Construction Economic Research and Professor at Alleghany College, Report for Pharmaceutical Industry Labor Management Association, September 2018*
26 *Based on 4Q2017 company announcements by AbbVie, J&J, Pfizer, Amgen, Merck and Eli Lilly*
27 *David Green, Maggie Zellers and Christine Chang, "Life Sciences Companies More Bullish on U.S. Investments Post Tax Reform," Deloitte Insights, October 26, 2018.*
28 *Avalere Health, Majority of API in US Consumed Medicines is Produced in the United States, Avalere Insights (Analysis Brief), July 15, 2020.*

rate of 12.5%, while also aggressively pursuing inward investments by international companies. Combined with Ireland's "Knowledge Development Box," under which manufacturers operating in Ireland may exclude from taxable income up to half the revenue from products linked to R&D performed in Ireland, that tax rate drops to an effective 6.25%.[29] The U.S. might also consider incentives for locating biopharmaceutical manufacturing facilities in distressed communities within states and territories. There is precedent for this type of incentive in the U.S. For example, prior to its repeal, section 936 of the tax code exempted U.S. manufacturing from corporate income taxes made in U.S. territories, helping to establish a significant biopharmaceutical manufacturing presence in Puerto Rico.

One incentive for innovation that must remain a centerpiece of U.S. policy is continuing to strengthen intellectual property and data rights and their enforcement both within America and abroad. Ensuring robust intellectual property protections is essential to provide the incentives for private investment to undertake the lengthy, costly, and risky R&D and manufacturing investments necessary to development new treatments and scale-up production. This needs to include support for comprehensive patent rights and adequate remedies for enforcement of patents, especially abroad. The U.S. International Trade Administration points out many growing impediments in intellectual property protection relating to the pharmaceuticals sector, including:[30]

- Patent backlogs and long, uncertain approval timelines are common problems worldwide with many countries lacking patent term adjustment provisions or ways to address unreasonable patent examination delays
- A number of [other nations'] regulatory bodies require large, and some would say excessive, amounts of data requirements at the time of filing to prove patentability
- Many countries lack early dispute resolution mechanisms and may even have policies that discourage companies from pursuing patent claims
- Countries are increasingly restricting the permissibility of post-filing data submissions, adding enormous uncertainties, costs and marketing delays for companies

> [N]ot only do IP instruments such as patents encourage innovators to invest in R&D and to commercialize their technologies, they also promote the disclosure and dissemination of knowledge that creates a platform upon which others can innovate, making the IP system, as James Madison described it, "one where the public good fully coincides with the interest of the innovators … Ultimately, IP does not represent an impediment to access to medicines; rather, in the vast majority of cases, it's the reason for the very existence of those medicines in the first place.
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> **Stephen Ezell, Ensuring U.S. Biopharmaceutical Competitiveness, ITIF, July 2020, page 33**

29 *https://www.revenue.ie/en/companies-and-charities/reliefs-and-exemptions/knowledge-development-box-kdb/index.aspx.*
30 *International Trade Administration, "2016 Top Markets Report Pharmaceuticals: Overview and Key Findings," U.S. Department of Commerce, pages 6-8*

Examples of Public-Private Biopharmaceutical Partnerships Across the World

Ireland: National Institute of Bioprocessing Research and Training
Ireland's NIBRT seeks to engage with all significant biomanufacturing players and is funded by IDA Ireland, the nation's inward-investment promotion agency. NIBRT is operated by a consortium of universities and its facilities are designed to replicate a modern bioprocessing plant with state-of-the-art equipment. (see https://www.nibrt.ie)

Saudi Arabia: Vaccine and Biomanufacturing Centre
A biomanufacturing facility offering shared access to single-use biomanufacturing technology is being opened at the research park attached to the King Abdullah University of Science and Technology. The center functions as a partnership among a private vaccine company, the national applied-research institute, and government agencies promoting startups and cluster development. (see https://innovation.kaust.edu.sa/agreement-signed-for-building-of-saudivax-rd-vaccine-center/)

Sweden: AdBIOPRO
Started with a grant from the state agency for innovation in the industrial setting, the Competence Centre for Advanced Bioproduction by Continuous Processing is hosted by the Royal Institute of Technology and governed by a joint academic/industrial board. Its goals include providing Swedish industry with distinct competitive advantages in biomanufacturing technologies and training highly qualified operating personnel. (see https://www.kth.se/adbiopro)

Australia: Advanced Biologics Manufacturing Facility
Complementing laboratory-scale facilities already in place, Australia's national laboratory (the Commonwealth Scientific and Industrial Research Organisation, or CSIRO) is opening a much larger cGMP Advanced Biologics Manufacturing Facility capable of producing proteins at high enough volume to support companies conducting Phase II drug trials. (see https://www.csiro.au/en/Research/MF/Areas/Biomedical/cGMP)

France: Shared Manufacturing Platforms at Regional Clusters
Two of France's regional biotech clusters have created shared platforms for biomanufacturing. At Lyon, a contract-manufacturing subsidiary of the nonprofit Institut Merieux is sharing its cGMP facilities with rising startups. Near Paris, the public vocational institute IMT offers apprenticeship training in biomanufacturing in collaboration with academic and industrial partners. (see https://www.genopole.fr/A-strategic-direction-for-Genopole.html?lang=fr#.XxbxES05Rnk and https://accinov.com/accinov-by-lyonbiopole/. And https://www.groupe-imt.com/en/.)

South Africa: Biomanufacturing Industry Development Centre
The national laboratory known as the Council for Scientific and Industrial Research has opened a Biomanufacturing Industry Development Centre in Pretoria. It describes itself as a "hub for open innovation in biomanufacturing," offering small and medium-sized enterprises manufacturing competency from lab-scale through pilot-scale manufacturing. (see https://biomanufacturing.csir.co.za/?page_id=576)

- Many countries do not provide adequate, if any, regulatory data protection or provide protection only for small molecule treatments but not for biologic medicines.

The value of intellectual property protection has been demonstrated fully in advancing new treatments for COVID-19. Of particular note is that intellectual property protections have proven effective in enabling collaborations to take place between organizations with solutions to different pieces of the COVID-19 puzzle (even among traditionally competing firms). Innovators can work together, secure in the knowledge that robust IP protection enables the fruits of their individual R&D efforts to be contributed to advance a collaborative solution.

Promote Public-Private Collaborations to Advance Innovative Biomanufacturing Technologies:

Continued innovation in manufacturing technologies is critical for the U.S. to overcome its high-cost environment and remain globally competitive in and continue to grow its biopharmaceutical manufacturing presence in the U.S. International competitors are actively increasing public-sector investments and advancing public-private partnerships to provide their local biopharmaceutical manufacturers a competitive advantage. In reaction to COVID-19, countries have significantly expanded public policies to increase investments as a means to strengthen the supplier base and are centerpieces of their comprehensive industrial policies.

A wide range of nations – Sweden, France, Australia, Saudi Arabia, and South Africa, for example – are making government-funded investments in pilot-scale manufacturing facilities to serve as open-innovation platforms linking clusters of innovative startups to large, established pharmaceutical companies.

One of the most prominent efforts is Ireland's National Institute of Bioprocessing Research and Training (NIBRT), which seeks to engage with all significant biomanufacturing players and is funded by IDA Ireland, the nation's inward-investment promotion agency. NIBRT is operated by a consortium of several universities in Dublin, and its facilities are designed to replicate a modern bioprocessing plant with state-of-the-art equipment.[31] It has a research agenda focused on cell biology and engineering; bioanalytics; advanced manufacturing; and bioinformatics and data analytics.[32] The NIBRT seeks funding from the EU, has several global university partnerships, and also performs proprietary contract research and consulting for industry.[33] It also includes an extensive program in education and training (both physical and online) for undergraduates, postgraduates, and industry employees seeking continuing education.[34] Ireland's investments in the NIBRT and related university-based activities earlier on the R&D spectrum seek to build ties between companies making inward investments in biomanufacturing and the Irish innovation ecosystem that are stronger than those based on tax advantages alone, and which thus create a "stickiness" of these investments over time.

Even before the COVID-19 pandemic, the U.S. has focused on public-private partnerships to address key R&D and other challenges. For example, FDA's Emerging Technology Program promotes the adoption of innovative approaches to pharmaceutical product design and manufacturing by facilitating collaboration between manufacturers and FDA to resolve potential technical and regulatory issues prior to filing a regulatory submission. Meanwhile, the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), one of fourteen Manufacturing USA Institutes of Manufacturing Innovation, connects companies, academic institutes, non-profits, and government entities to stimulate leadership in advanced biopharmaceutical manufacturing. NIIMBL has raised $125 million in private investment to match $70 million in federal funding. These investments are small, however, relative to the size of the U.S. biopharmaceutical industry, suggesting that they could be significantly ramped up.

To address the COVID-19 pandemic, public-private partnerships have become a centerpiece of the U.S. response. Through Operation Warp Speed, an unprecedented partnership between the federal government and the biopharmaceutical industry is taking place to accelerate the development, manufacturing and distribution of promising vaccines and therapeutics against COVID-19, while maintaining rigorous standards for safety and efficiency.[35] Of particular note is the significant level of federal investments to support expansions in manufacturing capacities for promising vaccine candidates while they are still in development, which gives biopharmaceutical companies the confidence to invest aggressively in development and ensures rapid access to supplies of newly approved vaccines for Americans. According to the factsheet on Operation Warp Speed, nearly $12 billion in funding for the development and manufacturing of vaccines for COVID has been made to more than ten companies involved in advancing new vaccines or manufacturing capacities for COVID vaccines.[36] Plus, Operation Warp Speed is supporting the development and manufacturing of three monoclonal antibody treatments.

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31 https://www.nibrt.ie/about/.
32 https://www.nibrt.ie/research/.
33 https://www.nibrt.ie/contract-research/.
34 https://www.nibrt.ie/wp-content/uploads/2020/02/Nibrt-Training-Catalogue-2020-13.pdf.
35 U.S. Department of Health and Human Services, "Explaining Operation Warp Speed," https://www.hhs.gov/sites/default/files/fact-sheet-operation-warp-speed.pdf
36 See U.S. Department of Health and Human Services explanation of Operation Warp Speed at https://www.hhs.gov/sites/default/files/fact-sheet-operation-warp-speed.pdfSlaoui, Moncef; Hepburn, Matthew (2020-08-26). "Developing safe and effective covid vaccines — Operation Warp Speed's strategy and approach". New England Journal of Medicine. 383 (18): 1701–1703.

Address Shortfalls in Stem Talent:

Perhaps the most significant long-term barrier to growth for the U.S. biopharmaceutical manufacturing industry and its broader innovation ecosystem is access to a robust STEM worker pipeline. The STEM skills gap is estimated to leave 2.4 million positions unfilled in the U.S. between 2018 and 2028, with a potential economic impact of $2.5 trillion. India and China produce almost half of all science and engineering bachelor's degrees, compared to American S&E bachelor's degrees which comprise only 10% of the global total.[37] For an economy that is highly dependent upon STEM talent, the U.S. is simply not making the grade, and this has important implications for STEM-dependent biopharmaceutical manufacturing as well.

International competitors are significantly outperforming the U.S. The Bloomberg Innovation Index, which examines more than 200 global economies across many dimensions of innovation, ranks the U.S. 47th in post-secondary efficiency.[38] This considers factors such as college enrollment rates, graduation rates, educational attainment, and science and engineering graduates as a share of all college graduates.

It is not only post-secondary education that is falling short in the U.S. Elementary and middle school students in the U.S. place among the lower end internationally in math and science assessments. Among 9th graders, the U.S. ranked 18th in science and 37th in math in the comprehensive and rigorous international assessment of student learning outcomes, known as PISA.[39]

Of particular concern for the U.S. are the persistent achievement gaps among students of color. Despite test-score improvements across all races for 8th grade students from 1990 to 2017 in the National Assessment of Education Progress, the average NAEP math scores among Black and Hispanic 8th graders in 2017 were lower than the average scores for White students in 1990. The College Board, meanwhile, finds that Blacks and Hispanics are far less likely than others to take advanced placement courses in math and science, which demonstrate academic preparedness for college. For those Black and Hispanic students who do take the AP, they score lower than White students.[40] This K-12 racial achievement gap carries through to post-secondary and results in a lack of diversity among college students pursuing STEM fields.

> Education levels required for manufacturing are rising, in part, due to the growth in large molecule (biologic) manufacturing. Whereas a high school diploma used to be sufficient to secure some biopharmaceutical manufacturing positions, now an associate's degree, or a high school diploma plus some relevant studies or certification, is generally the standard for a biopharma manufacturing operator.
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> **Deloitte, Advanced Biopharmaceutical Manufacturing: An Evolution Underway, 2015**

Over the years, U.S. biopharmaceutical companies have put in place a host of initiatives aimed at addressing the talent shortfall. A recent report by STEMconnector describes the many layers of the STEM workforce talent gaps seen in the U.S. These are presented in the following table, along with examples of how the biopharmaceutical industry is addressing these gaps.[41]

Industry actions alone, however, are unlikely to fully address the STEM gap in the U.S. workforce. Over the last decade, coalitions of experts and stakeholders from across education, research, medicine, industry, and labor have urged for increased public investment to grow our nation's STEM workforce. One prominent example is the Council for American Medical Innovation, which has proposed the following:

- Provide federal support for the biosciences in K-12 STEM efforts, including bioscience teacher preparation and professional development. Tactics should include more

37 *https://www.nsf.gov/statistics/2018/nsb20181/report/sections/overview/workers-with-s-e-skills)*
38 *Michelle Jamrisko, Singapore Leaps Up the Rankings in Bloomberg's Innovation Index, Bloomberg, January 20, 2020*
39 *OECD, "United States PISA 2018 Results Country Note," December 2019*
40 *Inside Higher Education, "More AP Success; Racial Gaps Remain," February 2019*
41 *STEMconnector, State of STEM: Defining the Landscape to Determine High-Impact Pathways for the Future Workforce, 2018.*

extensive recruitment of biology majors to enter teaching, alternative certification of biomedical professionals, and summer stipends to universities for professional development for existing teachers.

- Provide funding to vocational and technical schools and community colleges to establish, in concert with industry consortia, programs to retrain existing workforce for biomedical careers.

- Increase the number of U.S. and foreign students pursuing graduate degrees and careers in the biosciences in the United States. Strategies may include scholarships and loan forgiveness for U.S. students pursuing degrees in biology, chemistry, engineering, and related majors and a streamlined green-card application process for foreign graduates of U.S. universities at the master's and Ph.D. levels.

Time is of the essence in addressing our nation's talent shortfall. Nothing short of a comprehensive and collaborative approach of industry, education and government working together with students and their families will fully tackle this critical need.

Table 1: Identified Gaps in the STEM-ready Workforce and Examples of Industry-Supported STEM Programming Addressing Each

Identified STEM Gaps	Examples of Industry-Supported STEM Programming Addressing Gap
Skills: not enough students or young people are developing the fundamental skills needed to succeed in STEM careers.	Deep summer learning and research experiences, hands-on lab experiences, science fairs, and industry-grade equipment donations all contributing toward scientific "hard" skills required in STEM careers.
Biases or "Belief" Gap: students and the adults around them, including school counselors and teachers, hold incorrect biases about the aptitude or traits young people must have to belong and thrive in STEM fields. Low-achieving students often overlooked.	Biopharmaceutical companies are engaging students at all achievement levels, especially in formative K-12 years of schooling. Hands-on engagements in science fairs, classroom and industry site visits designed to demonstrate students from all backgrounds have a potential future in the industry or in broader STEM fields.
Postsecondary Education: the knowledge economy requires credentials beyond a high school diploma, but not enough young people are earning those credentials, nor are they earning credentials that are relevant to industry needs.	Industry is sponsoring numerous scholarships for post-secondary degree programs in industry-relevant academic fields.
Geographic Gap: access to jobs in high-growth and well-paid fields often depends on geography. Hubs of economic growth may be far from large concentrations of qualified job seekers, or they may be far from population centers.	The industry supports a breadth of national programs offered regardless of state or locality, in addition to programs offered across 29 states, DC and Puerto Rico. These programs provide valuable resources to families and schools in urban, suburban, and rural areas alike.
Demographics: there is a well-documented, disproportionate lack of participation in STEM education and careers among people of color and women, despite a significant focus on diversity and inclusion.	37 industry-supported programs, or just over half of those reported in the survey, are designed to intentionally inspire and engage underrepresented population groups.

Source: STEMconnector, State of STEM, 2018.

Charting A Bright Future for U.S. Biopharmaceutical Development

The strength, resiliency and responsiveness of the U.S. biopharmaceutical manufacturing industry has been critical to ensuring a robust response to the COVID-19 pandemic both in terms of avoiding supply chain disruptions and ensuring continued patient access to medicines and vaccines and in increasing manufacturing capacity and ramping up production at the same time that biopharmaceutical researchers are researching and developing potential new treatments and vaccines to counter the virus. The U.S. biopharmaceutical manufacturing industry's global leadership has is helping our nation to meet the current and projected demands posed by the COVID-19 pandemic, but our ability to remain a global leader in biopharmaceutical manufacturing cannot be taken for granted. The U.S. confronts significant headwinds due to significantly higher costs of production compared to global competitors and the fact that the rest of the world is making significant investments to increase their capacities and implement policies to attract private sector R&D and manufacturing facilities to sustain and grow their economies and support their efforts at long-term pandemic preparedness.

Assessing the favorability of the policy and regulatory environment to support the biopharmaceutical manufacturing ecosystem in the U.S. compared to other countries is critical important to identifying gaps that need to be addressed to sustain and grow manufacturing in the U.S. Having public policies that provide robust incentives for R&D and manufacturing investments is critical not just to U.S. economic growth but also in ensuring we as a country are well positioned for the next pandemic.

Still, another part of the equation for success is doing no harm. Despite the fact that 75 percent of the spending on drugs in the U.S. are for products manufactured within the U.S. and there is no over-reliance on China or any other single nation for pharmaceutical supplies, there are calls for "buy American" mandates for medicines, particularly active pharmaceutical ingredients (APIs). The problem, as explained by Professor Willy Shih of the Harvard Business School and an expert on manufacturing, is that these APIs like many other imported supplies are commodities and forcing production in the U.S. will raise the cost of drug prices without the benefit of creating a more resilient supply chain. In fact, such mandates risk creating shortages by disrupting supply chains that have functioned well through the COVID-19 pandemic for essential medicines and reduce access to multiple sources of supply that are needed for a high-functioning supply chain.[42] These mandates also invite retaliatory action by other nations and could actually undercut exports of medicines by the U.S., which according to the U.S. International Trade Administration "rank as one the top exporting sectors for IP-intensive industries in the United States."[43]

The alternative that Professor Shih recommends is having the U.S. government work together with manufacturers to invest in process innovations, advance biomanufacturing capacities and streamline regulatory approaches in regards to the supply chain to reduce barriers of entry for new suppliers. These are the types of pro-active public policies that are needed to shore up the competitiveness of America's global leadership in biopharmaceutical manufacturing industry.

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42 Willy Shih, "Companies that Want to Make Pharmaceutical APIs will be Producing Commodities. Here's What They Should Consider," Forbes, July 29, 2020
43 International Trade Administration, "2016 Top Markets Report Pharmaceuticals: Overview and Key Findings," U.S. Department of Commerce, page 4


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