

# Ensuring U.S. Biopharmaceutical Competitiveness

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If the United States is serious about maintaining its leadership in biopharmaceuticals, then it's time for policymakers to articulate and embrace a robust sectoral competitiveness strategy.

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## KEY TAKEAWAYS

- The biopharmaceutical industry makes important contributions to the U.S. economy, including employing over 500,000 workers making 1.4 times the U.S. earnings average.
- The United States leads the world on most indices of R&D investment and innovation. From 2004 to 2018, U.S.-headquartered firms produced almost twice as many new drugs as did firms in Europe, and 3 to 4 times as many as Japan.
- Despite U.S. strengths in biopharmaceutical R&D and innovation, manufacturing has dropped. From 2009 to 2018, real value-added output in pharmaceutical and medicines manufacturing fell by nearly one-third.
- Partly as a consequence, the U.S. trade balance in pharmaceuticals has grown from a deficit of \$16 billion in 2010 to a deficit of \$77 billion in 2019.
- Calls for reshoring more biopharmaceutical manufacturing should distinguish between mature manufacturing processes and those still evolving, as in continuous process biomanufacturing, where U.S.-based production can enjoy unique strengths.
- America must continually bolster its biopharmaceutical leadership position, especially as China implements ever-more aggressive policies to improve their life-sciences competitiveness, not only in production but also in innovation.
- To support the sector, policymakers should focus on: 1) maintaining strengths, including in pricing, tech transfer, and intellectual property; 2) spurring domestic innovation; 3) spurring increased domestic production; and 4) combatting foreign mercantilism.

## INTRODUCTION

Nations are competing for increased market share in a wide array of advanced-innovation industries, understanding that these industries are the key to competitiveness, national security, and good jobs. China's "Made in China 2025" strategy is perhaps the most visible of these efforts, but by no means the only one.

Many nations, including China, have targeted the biopharmaceuticals industry—an industry which the United States has long led—especially in drug innovation. One result has been that over the last decade U.S. biopharmaceutical manufacturing value-added output has fallen by almost one-third, as the U.S. trade deficit in drugs and inputs has increased. Fortunately, America still leads in innovation and drug development, in large part due to effective life-science policies, including significant federal investment in life-sciences basic research, robust intellectual property (IP) protections, effective technology transfer policies, investment incentives, and, importantly, drug pricing policies that enable companies to invest in high-risk drug development.

But if the story of the past decline, and even loss, of other critical U.S. industries provides any guide, loss of U.S. production will ultimately lead to the loss of innovation capabilities as well.<sup>1</sup> It is not enough for the United States to lead in drug development, it must also at least hold its own in drug production. This is especially true given the coming challenge from China, which intends to dominate the global drug industry, at all phases, from innovation to production to marketing.

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**If the United States is serious about biopharmaceutical competitiveness, an industry that it still has strong capabilities in—unlike the telecom equipment or flat-panel display industries, to name just two—then it's time for Washington to articulate and embrace a robust national biopharmaceutical competitiveness strategy.**

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Now is not the time for free-market complacency, hoping that America's entrepreneurial spirit and rule of law will somehow suffice (the United States didn't gain its biopharma lead from a laissez faire approach, and it certainly won't keep its lead with it alone). Nor is it the time for drug populism, a political movement that both sides of the aisle, but especially progressives, have unfortunately embraced. Drug populism and its accompanying policies of weaker IP protections and draconian drug price controls would likely result in cheaper drugs. But there should be no confusion that it will lead to a hollowing out of U.S. capabilities, not just in production but also in innovation (and, not to mention, fewer new lifesaving drugs). If the United States is serious about competitiveness overall, and competitiveness in the biopharma sector specifically, an industry that the United States still has strong capabilities in—unlike the telecom equipment or flat-panel display industries, to name just two—then it's time for Washington to articulate and embrace a robust national biopharmaceutical competitiveness strategy.

This report begins by examining the importance of America's biopharmaceutical industry to the country's health and economy, assesses its competitiveness in a global context, explores

challenges to America's leadership, and offers a policy roadmap designed to ensure America remains the world's life-sciences innovation and production leader.

Policy recommendations include:

### Maintain U.S. Strengths

- The Trump and future administrations should not introduce drug price control schemes, such as the Department of Health and Human Services' (HHS) proposed International Pricing Index Model for Medicare Part B Drugs.
- The National Institute of Standards and Technology (NIST) should affirm that price is not an adequate basis for the exercise of march-in rights under the Bayh-Dole Act.
- Congress should reauthorize the Prescription Drug User Fee Act (PDUFA) when renewal comes up in 2022, and continue to incorporate innovation-enhancing elements to it.
- The U.S. Treasury should apportion any withheld user fees to the U.S. Patent and Trademark Office (USPTO) with alacrity to fund continued, uninterrupted USPTO operations.

### Expand and Adopt New Policies to Spur Greater Domestic Innovation

#### Research & Development Funding

- Congress should at least restore National Institutes of Health (NIH) funding to 2003 levels as a share of gross domestic product (GDP), which would entail boosting NIH funding by \$11.6 billion annually.
- Congress should close the federal research and development (R&D) underinvestment gap in the life-sciences and other sectors by passing the bipartisan Endless Frontiers Act.
- The Department of Commerce should promote the creation of R&D megafunds by establishing an office to develop and implement the needed incentives and oversight for the creation of megafunds.

#### Investment Incentives

- Congress should at least double the Alternative Simplified R&D tax credit.
- Congress should amend the existing collaborative R&D tax credit to allow companies to take a flat 20 percent tax credit when they invest in university R&D activity.
- Congress should stimulate further investment in rare-disease R&D and innovation by restoring the orphan drug tax credit to 50 percent.
- Congress should amend Section 469 of the tax code to permit passive investors to take advantage of the net operating losses and research tax credits of the companies in which they invest.

#### Supporting Data-Driven Drug Development

- Congress should direct HHS to implement a unique patient identifier, as originally intended by the Health Insurance Portability and Accountability Act (HIPAA).
- Policymakers should enforce the publication of data from clinical trial results by directing agencies such as the Food and Drug Administration (FDA) and NIH to be more aggressive about penalizing noncompliance.

- Congress should direct HHS to create a model for data trusts that facilitates data sharing among biopharmaceutical stakeholders involved with data-driven drug development.
- Congress should increase the availability of new kinds of data from nontraditional sources, such as biometric, lifestyle, and environmental data, to aid the drug-development process, such as by ensuring NIH provides adequate funding supporting the All of Us Research Program's million-person research cohort.
- Congress should direct the FDA to develop best practices for data collection in health care to ensure equitable outcomes.
- Congress should ensure the FDA has the resources necessary to increase foreign clinical trial inspections, harmonize regulatory standards across national lines to meet the agency's satisfaction, and adopt risk-assessment analytics tools to prioritize inspections for high-risk sites.

### **Expand R&D Talent**

- Congress should appropriate \$20 million per year for the establishment of a National Science Foundation (NSF)-Industry Ph.D. Fellows Program, to support an additional 1,000 Ph.D. students in STEM (science, technology, engineering, and mathematics) fields.
- Congress should make it easier for foreign graduates with a STEM degree to receive a green card.
- The federal government should not restrict L-1 visas.

### **Collaboration to Increase Efficiency in Drug Development**

- Federal support for joint industry-university research efforts in biopharma R&D efficiency and effectiveness should be expanded.

### **Support Policies to Spur Increased Domestic Production**

#### **Support R&D for Biopharma Process Innovation**

- Congress should significantly expand funding for biomedical Manufacturing USA centers, including for the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), as well as establish other centers that address related manufacturing technology challenges.
- Federal funding for NIIMBL and the other Institutes of Manufacturing Innovation that constitute the Manufacturing USA network should be ongoing and not sunset.
- Congress should fund NSF to both expand support to university-industry research centers working on biopharmaceutical production technology and establish new centers.
- Congress should increase funding for NSF's Division of Engineering, and target much of the increase to the Chemical Process Systems Cluster and Engineering Biology and Health Cluster.
- The administration should encourage the creation of the biopharma equivalent of the Semiconductor Research Corporation, a public-private consortium dedicated to developing long-term industry R&D and technology development roadmaps.

- The industry should collaborate on a production technology innovation roadmap, and the federal government should match industry funding to research institutes and universities on a dollar-for-dollar basis.
- Congress should establish an investment tax credit for new manufacturing facilities and equipment in the United States.
- Congress should expand the Manufacturing Engineering Education Grant program from its current \$15 million annual funding and direct the Department of Defense (DOD) to develop a competition for biomedical manufacturing programs.
- Congress should expand funding for NSF's Advanced Technical Education program and target the funds to the development of centers focused on industry skill needs.

### **Create Incentives for Domestic Production**

- Congress should task the administration with developing a national medical products strategy that would identify key vulnerabilities in biopharmaceutical and medical-product supply chains and develop solutions, where appropriate, to encourage reshoring or promote greater levels of domestic manufacturing at home.
- Congress should create the equivalent of the CHIPS (Creating Helpful Incentives to Produce Semiconductors) Act and American Foundries Act, legislation supporting the expansion of U.S. semiconductor production, for the biopharmaceutical industry. This would include allocating at least \$5 billion per year to states (matched at least with 50 cents in state funding for every \$1 in federal funding) to provide incentives for the establishment of new biomedical production facilities in the United States.
- Congress should restore the tax credit for biopharma production in Puerto Rico and other U.S. territories.

### **Reform Regulations of Biomedical Production**

- Congress and the administration should continue to work with the FDA to streamline and accelerate the agency's capacity to evaluate and approve innovative new pharmaceutical manufacturing processes.

### **More Aggressively Contest Foreign Biopharmaceutical Mercantilism**

- A key objective of U.S. trade policy should be to prevail on America's trade partners to appropriately value innovative medicines.
- Congress should use the opportunity of Trade Promotion Authority (TPA) renewal to affirm that a key priority of U.S. trade policy should be that America's trade partners pay their fair share for innovative drugs.
- U.S. trade policy needs to resist the mistaken view that IP is not a trade policy issue. At a minimum, U.S. administrations should continue to seek at least 10 years of data exclusivity in Federal Trade Agreements (FTAs), including the FTA currently being negotiated with the United Kingdom and also the Comprehensive and Progressive Trans-Pacific Partnership (CPTPP), which the next presidential administration should seek for the United States to join.
- The United States Trade Representative's (USTR) Office should continue to contest countries' data localization practices and restrictions on genomic data movement as well

as promoting rules, such as those in the United States-Mexico-Canada (USMCA) free trade agreement (FTA), that promote open data flows and proscribe data localization measures.

- U.S. policy should promote the development of an interoperable, integrated global digital health framework.

## **IMPORTANCE OF THE U.S. BIOPHARMACEUTICAL INDUSTRY**

The biopharmaceutical industry makes significant contributions to both America's health and economy. The following section examines both in turn.

### **Contribution to Health**

Medicines are critical to health. Since 2000, the FDA has approved more than 500 new medicines.<sup>2</sup> As of 2020, biopharmaceutical companies in the United States have more than 3,400 drugs under clinical development, accounting for almost half of the estimated 8,000 medicines under development globally (1,100 of which are being developed to treat various forms of cancers).<sup>3</sup> And while some have asserted that biotechnology companies focus too often on “me-too” drugs that compete with other treatments already on the market, the reality is that most of the drugs currently under development seek to tackle some of the world's most intractable diseases, including Alzheimer's, cancer, and communicable diseases. This includes 130 coronavirus vaccines under development globally as well as 144 active trials of coronavirus therapeutic agents, and another 457 development programs for new therapeutic agents, which the FDA is tracking through its Coronavirus Treatment Acceleration Program.<sup>4</sup>

Moreover, such arguments miss that many of the drugs developed in recent years have in fact been first of their kind. For instance, in 2014, the FDA's Center for Drug Evaluation and Research (CDER) approved 41 new medicines (the most since 1996 at that point), many of which were first-in-class medicines, meaning they represent a possible new pharmacological class for treating a medical condition.<sup>5</sup> In that year, 28 of the 41 drugs approved were considered biologic or specialty agents, and 41 percent of medicines approved were intended to treat rare diseases. In 2018, CDER approved a record 59 novel drugs, and in 2019, 48 novel drugs, making 2019 the third-largest approval class in the past 25 years.<sup>6</sup> As of 2020, 74 percent of medicines in clinical development in the United States are potentially first-in-class medicines, including 86 percent for Alzheimer's, 70 percent for various forms of cancer, and 73 percent for cardiovascular diseases.<sup>7</sup>

Biomedical innovation generates a positive economic impact. Frank Lichtenberg found that pharmaceutical innovation accounted for 73 percent of the increase between 2000 and 2009 in life expectancy at birth in 30 countries (or 1.27 years of the 1.73-year increase in life expectancy).<sup>8</sup> Another study by Lichtenberg found that drugs launched since 1982 have added 150 million life-years to the lifespans of citizens of the 22 countries analyzed, with the average pharmaceutical expenditure per life-year saved being \$2,837.<sup>9</sup> A related study found that if no new drugs had been launched after 1981, the number of years of life lost would have been more than twice as high as it actually was.<sup>10</sup>

Further, Lichtenberg calculated that the years of life lost before the age of 85 in 2013 would have been 2.16 times as high if no new drugs had been launched after 1981.<sup>11</sup> For instance,

consider cancer: Since peaking in the 1990s, U.S. cancer death rates have declined by 27 percent.<sup>12</sup> Approximately 73 percent of survival gains in cancer are attributable to new treatments, including medicines.<sup>13</sup> The development of breakthrough drugs such as Imatinib for chronic myeloid leukemia (CML) has increased the five-year survival rate for CML patients to 89 percent, with many CML patients now living close-to-normal lifespans.<sup>14</sup> In fact, an individual with CML who has been treated with Imatinib and has been in remission for two years has the same life expectancy as someone who does not have cancer.<sup>15</sup> Likewise, Yervoy, a breakthrough treatment for patients with advanced metastatic melanoma that heralded the start of the cancer immunotherapy field using a technique known as checkpoint blockading, has enabled over one-quarter of patients to still be living at least 4.5 years after treatment.<sup>16</sup>

Thus, far from being the leading cause of rising U.S. health-care system costs, greater levels of life-sciences innovation will be key to limiting the growth of health-care system costs. Indeed, significant economic benefits could be achieved if innovative medicines could make progress toward addressing some of the most intractable diseases.<sup>17</sup> For instance, a 1 percent reduction in mortality from cancer would deliver roughly \$500 billion in net present benefits, while a cure could deliver \$50 trillion in present and future benefits.<sup>18</sup> Likewise, the financial impact of Alzheimer's disease is expected to soar to \$1 trillion per year by 2050, with much of the cost borne by the federal government, according to the Alzheimer's Association report "Changing the Trajectory of Alzheimer's Disease."<sup>19</sup> However, the United States could save \$220 billion within the first 5 years, and a projected \$367 billion in the year 2050 alone, if a cure or effective treatment to Alzheimer's disease were found. The potential economic opportunity associated with curing brain diseases and related disorders could be more than \$1.5 trillion per year—equivalent to 8.8 percent of GDP.<sup>20</sup>

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**Far from being the leading cause of rising U.S. health-care system costs, greater levels of life-sciences innovation over the long term will actually be key to limiting the growth of health-care system costs.**

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But even short of breakthrough cures, the economic benefits of pharmaceutical innovation are manifold. For instance, Lichtenberg found that "the value of reductions in work loss days and hospital admissions attributable to pharmaceutical innovation was three times larger than the cost of new drugs consumed."<sup>21</sup> Lichtenberg further found that the mean number of lost work days, lost school days, and hospital admissions declined more rapidly among medical conditions with larger increases in the mean number of new (post-1990) prescription drugs consumed.<sup>22</sup> He further found that "the use of newer prescription drugs also reduced the ratio of the number of workers receiving Social Security Disability Insurance benefits to the working-age population, and has had a positive effect on nursing home residents' ability to perform activities of daily living."<sup>23</sup>

U.S. health spending to treat major chronic diseases and conditions topped \$1.1 trillion in 2018.<sup>24</sup> Ideally, biopharmaceutical innovation can help bring down chronic-care costs by producing cures, as Gilead Sciences did when it introduced Sovaldi, offering a true cure for hepatitis C virus (HCV) patients, for whom the cost of treatment ranges from \$1 billion to \$2.3 billion per 10,000 HCV-infected patients, depending on the treatment regimen.<sup>25</sup> As Weiner and Lucas wrote, "Despite its cost, HCV treatment provides good value for the money, as expressed in



terms of cost-effectiveness.”<sup>26</sup> Overall, new hepatitis C cures have the potential to reduce future U.S. health care spending by \$115 billion.<sup>27</sup>

## Economic Contribution

As a sector that is globally traded (as opposed to non-traded sectors such as dry cleaners and barber shops), the biopharmaceutical industry makes important contributions to the U.S. economy not only by creating direct economic activity but also by supporting indirect activity. Pharmaceutical and medicine manufacturing accounted for 0.95 percent of private-sector value added in 2018.<sup>28</sup> Biotech R&D establishments accounted for another 0.23 percent.<sup>29</sup> The industry operates approximately 1,100 plants involved in the production of human-use medicines across 45 states and Puerto Rico.<sup>30</sup>

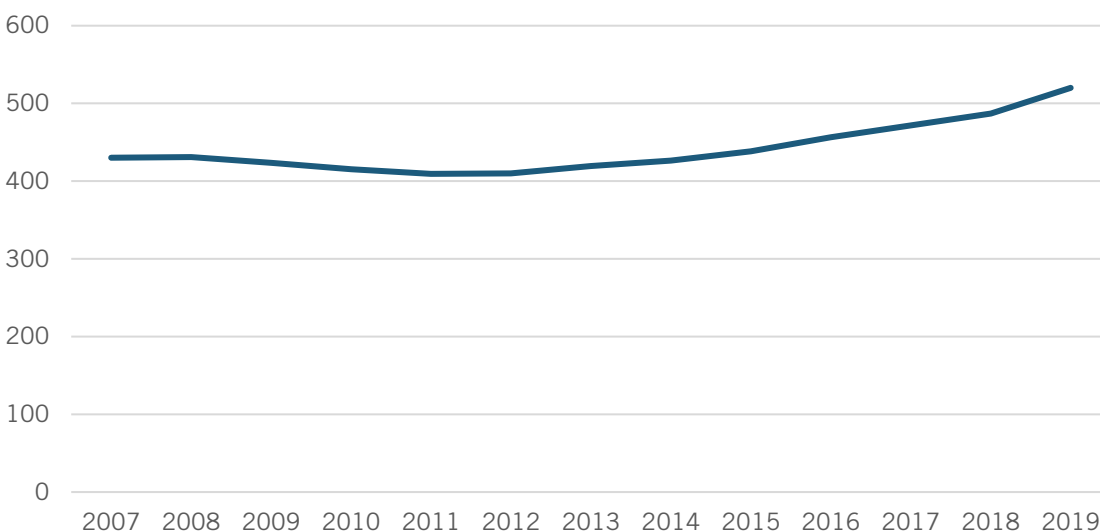
The industry also generates downstream economic impacts. Expenditures by 17 large biopharmaceutical companies made to suppliers in the United States amounted to more than \$58 billion in 2015.<sup>31</sup> And construction spending on 249 major new or upgraded R&D and manufacturing plants amounted to more than \$22.4 billion in 11 states from 2012 to 2017, with an estimated additional \$4 billion annually through 2020.<sup>32</sup>

## Employment Contribution

U.S. biopharmaceutical employment exceeded 500,000 employees as of May 2019, including 297,000 workers in pharmaceutical manufacturing and just over 200,000 biotechnology R&D workers. (See figure 1 and figure 2.) In addition, there are likely tens of thousands more workers employed in pharmaceutical R&D, however U.S. government statistics do not allow for the data to be broken out at that level. Examining the pharmaceutical sector alone, 71,000 (or 23.9 percent) of its workers were in STEM occupations, more than four times the national average of 5.7 percent. This ranks the pharmaceutical industry as the 6th-most-concentrated source of STEM workers out of 68 manufacturing industries, and 14th out of 244 industries overall.<sup>33</sup>

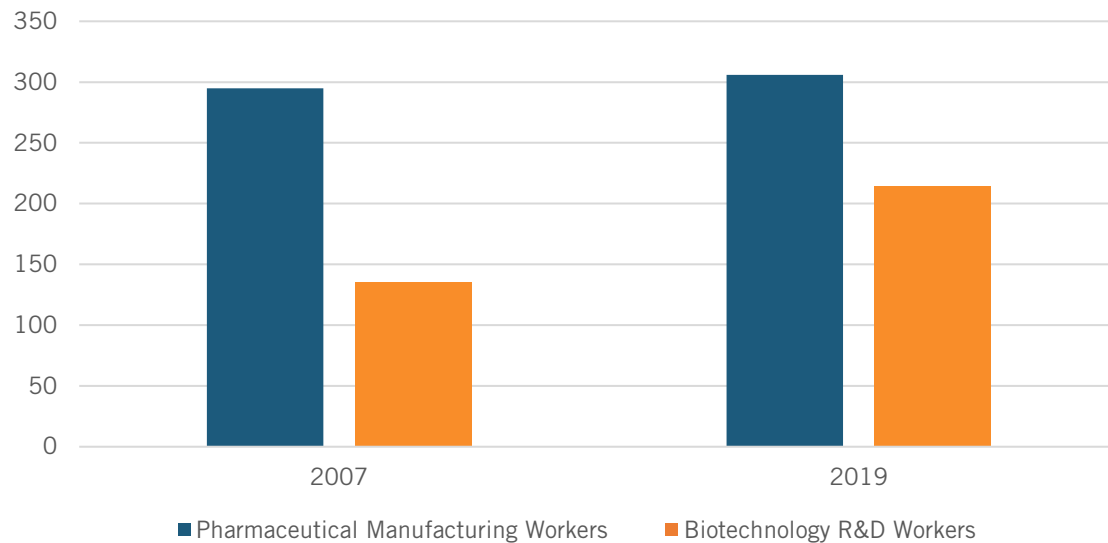
While every other U.S. manufacturing sector experienced job losses in the late 2000s, employment in the pharmaceutical industry fell a relatively small 3 percent from 2007 to 2010, and increased by over 25 percent from 2010 to 2019. (See figure 2.)

**Figure 1: U.S. biopharmaceutical employment (thousands)**<sup>34</sup>

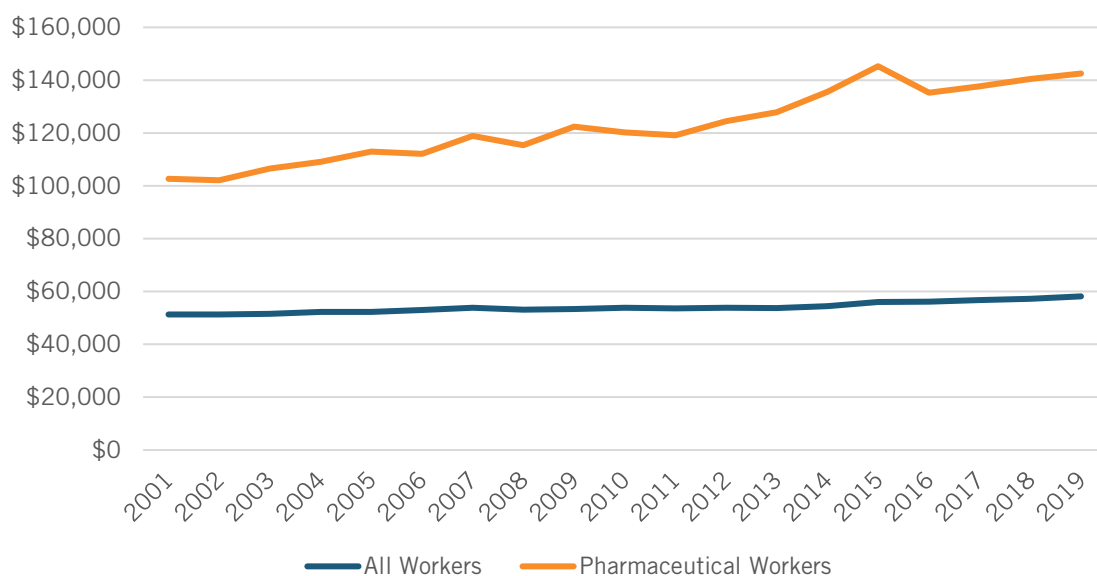




**Figure 2: Biopharmaceutical workers by industry, 2007 and 2019 (thousands)**<sup>35</sup>



**Figure 3: Real average wages in biopharmaceuticals and for all workers (2018 dollars)**<sup>36</sup>



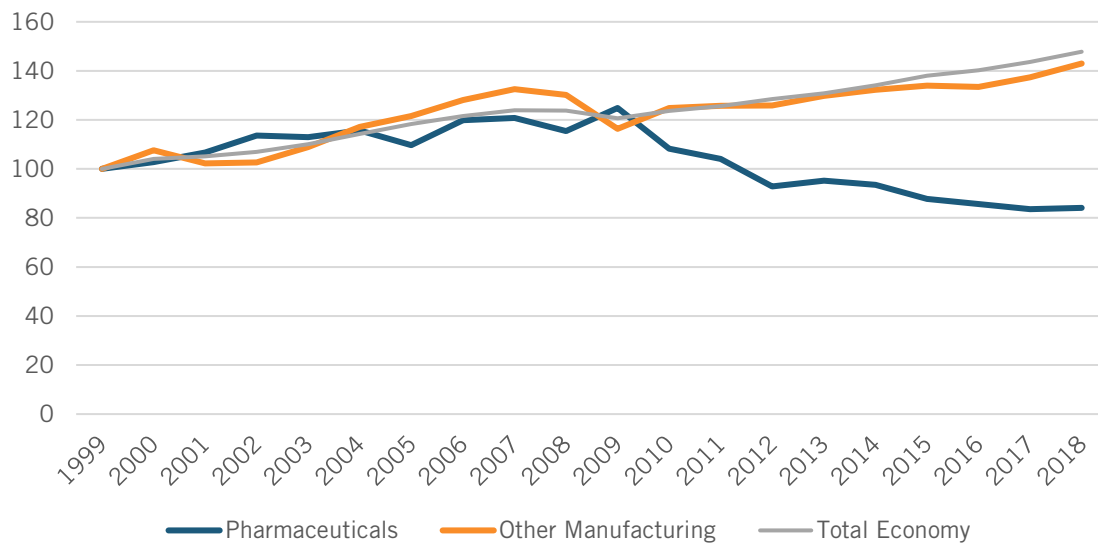
Many nations target competitiveness in the biopharmaceutical sector because it provides high-paying jobs. On average, wages for biopharmaceutical workers topped just over \$140,000 in 2019, compared with \$58,200 for all U.S. workers.<sup>37</sup> (See figure 3.) U.S. biopharmaceutical manufacturing jobs paid an average wage of \$117,700 in 2019, while biotechnology R&D-firm jobs paid an average of \$181,200 annually.

The industry also provides relatively well-paid jobs for workers without a college degree. In 2017, the industry employed 153,000 workers who did not have a college degree, at an annual average wage of \$50,900, 54 percent higher than the average wage for all non-college-educated workers.<sup>38</sup>

## Value-Added Economic Output

From 1999 to 2009, pharmaceutical and medicines manufacturing real (inflation-adjusted) value added grew faster than the rest of U.S. manufacturing: 25 percent versus 16 percent. But starting in 2009, the picture reversed. From 2009 to 2018, real value-added output fell by nearly one-third, while the rest of U.S. manufacturing increased by 23 percent.<sup>39</sup> (See figure 4.) (Value added is defined as the value of final sales minus inputs, such as raw materials, energy, etc.) One study found that “between 2013 and 2017 the United States lost about 22 percent of its drug manufacturing, while the number of foreign facilities selling to the United States declined by just 10 percent for active pharmaceutical ingredients (API) production and 3 percent for final drug production.”<sup>40</sup>

**Figure 4: Change in real value added for pharmaceutical and medicines manufacturing (1999=100)<sup>41</sup>**



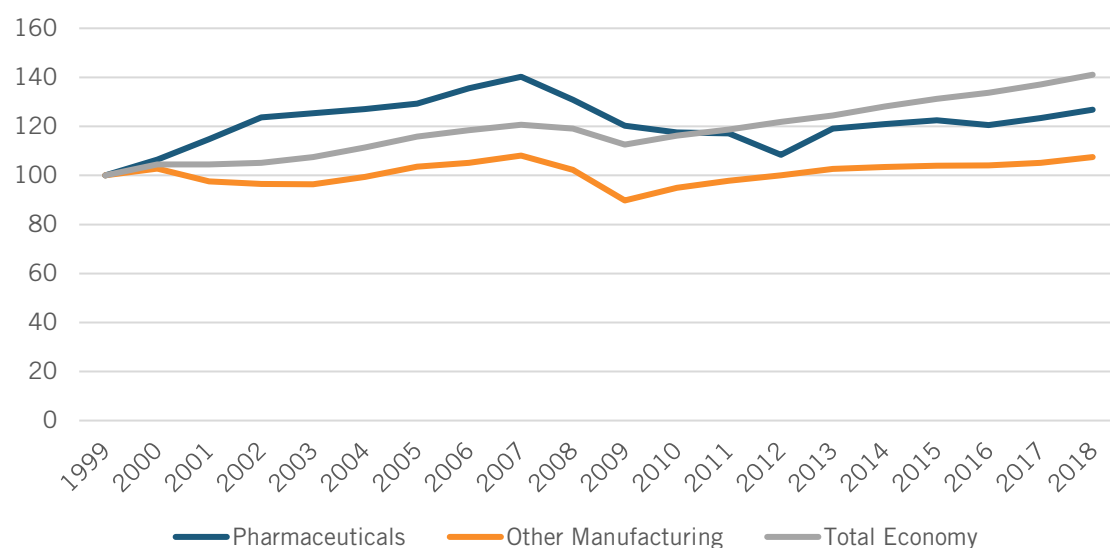
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In contrast, pharmaceutical change in real gross output increased by 20 percent from 1999 to 2008, and by 5 percent from 2008 to 2018, compared with a 10 percent decrease and 20 percent increase in other manufacturing over the same periods. (See figure 5.) This suggests that pharmaceutical producers in the United States have increased their revenues but have become increasingly reliant on importing more inputs than they had before.<sup>42</sup>

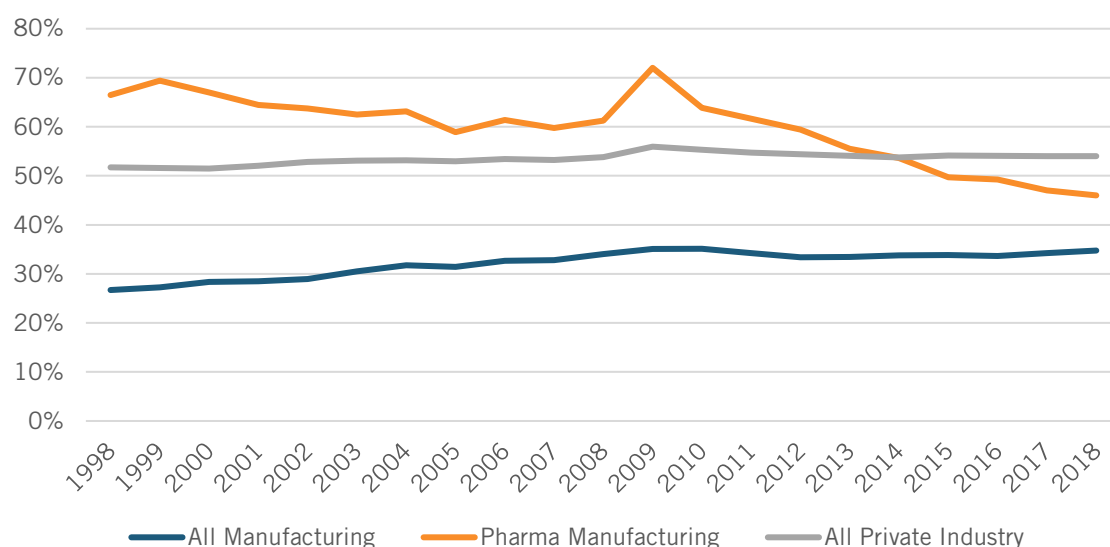
**Figure 5: Change in real gross output for pharmaceutical and medicines manufacturing (1999=100)<sup>43</sup>**



In terms of the ratio of value-added to gross output from 1998 to 2018, the ratio for overall manufacturing increased, but the ratio for pharmaceutical manufacturing fell, especially after 2009, consistent with the explanation that companies were relying more on foreign inputs, while there was little change in the overall economy over this time. (See figure 6.) Nevertheless, pharmaceutical manufacturing still remains a high value-added industry: In 2018, value added accounted for 46 percent of the industry's total output, compared with 35 percent for manufacturing overall.

**From 2009 to 2018, real (inflation-adjusted) value-added output in pharmaceutical and medicines manufacturing fell by nearly one-third, while the rest of U.S. manufacturing increased by 23 percent.**

**Figure 6: Ratio of real value added to real gross output as a share of GDP, 1998–2018<sup>44</sup>**



## R&D

The biopharmaceutical industry invests more in R&D than almost any other sector, yet it spends less on advertising than the U.S. industry average.<sup>45</sup> The industry invests on average over 20 percent of its sales in R&D since 2000.<sup>46</sup> In 2017, the pharmaceuticals and medicines industry invested \$104.8 billion in worldwide research, of which 64 percent was performed by the companies themselves and the rest by others, including universities.<sup>47</sup> In 2017, the industry conducted \$78.2 billion in worldwide research, with this amount complemented by an additional \$6.4 billion in biotechnology R&D. Industry-funded, U.S.-conducted pharmaceuticals and medicines R&D investment increased from \$12.2 billion in 1999 to \$66 billion in 2017.<sup>48</sup> Half of company-funded biopharmaceutical research was performed by companies with 10,000 employees or more.<sup>49</sup>

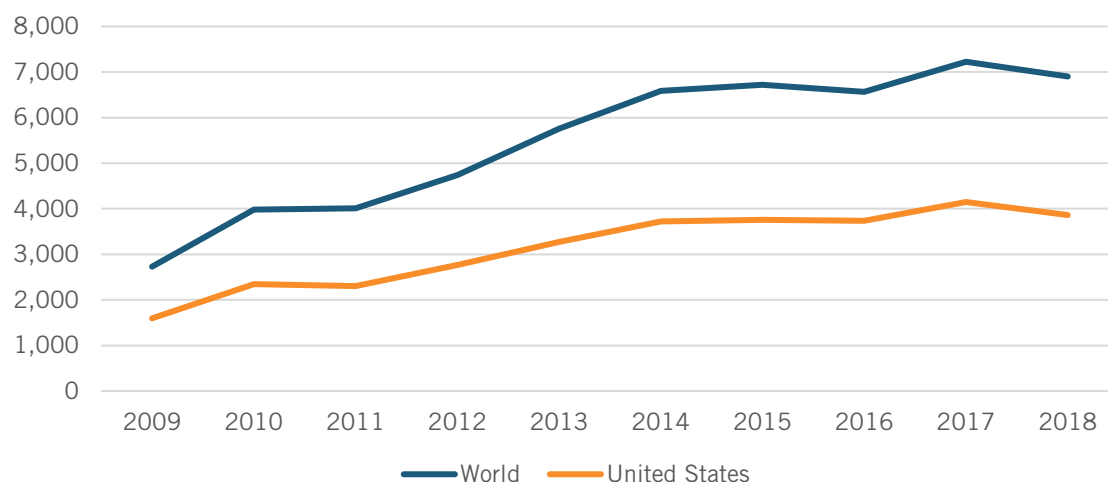
Total biopharmaceutical R&D investment (company-funded and other) in 2017 equaled 21.9 percent of domestic sales, over four times greater than the average for all U.S. industries, at 4.9 percent.<sup>50</sup> The sector accounted for almost 17 percent of U.S. business R&D performance, vying that year for the lead with computer and electronic products manufacturing (which accounted for 20 percent).<sup>51</sup>

Moreover, while the industry accounts for 16.8 percent of all U.S. business R&D, it accounts for 61 percent of all business R&D funding of universities.<sup>52</sup> For example, many of the U.S. universities that receive the largest share of their R&D support from industry—including Duke, the University of Alabama at Birmingham, University of Texas MD Anderson, and the University of Pennsylvania—have world-leading biomedical research programs.<sup>53</sup>

## Patenting

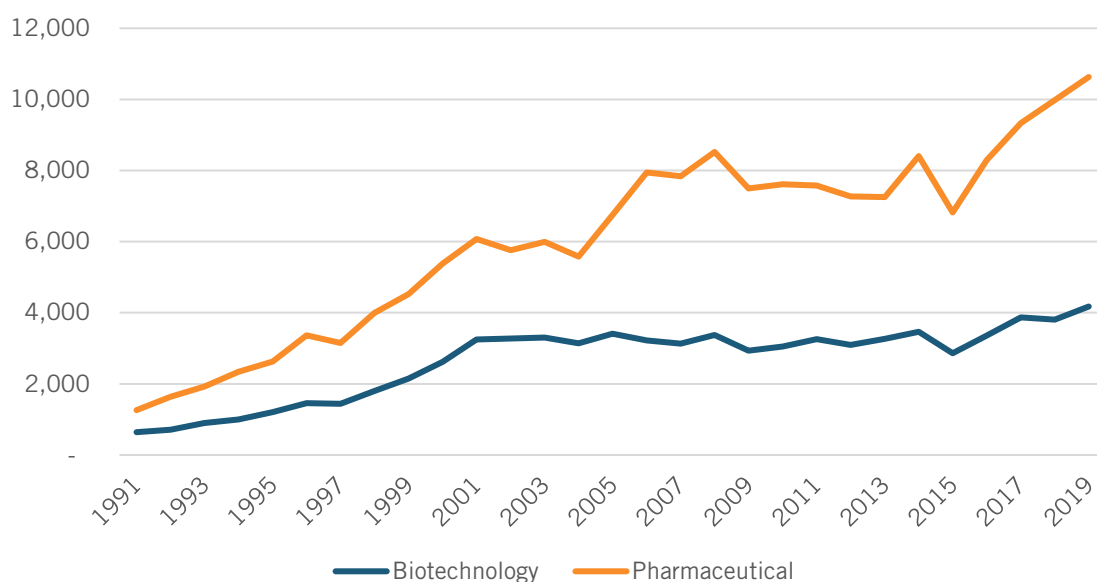
From 2009 to 2018, life-sciences patents issued by the USPTO to U.S. inventors increased 142 percent, from 1,597 in 2009 to 3,863 in 2018. (See figure 7.) However, patents issued to foreign inventors grew at a faster rate, 168 percent, over this time.

**Figure 7: USPTO-issued pharmaceutical patents, 2009 to 2018<sup>54</sup>**



The number of U.S. pharmaceutical patent applications to USPTO increased over eight-fold from 1,261 in 1991 to 10,630 in 2019, while the number of U.S. biotechnology patent applications increased 6.5-fold, from 641 to 4,175 over that time period. (See figure 8.)

**Figure 8: Number of U.S. life-sciences patent applications to USPTO, 1991–2019**

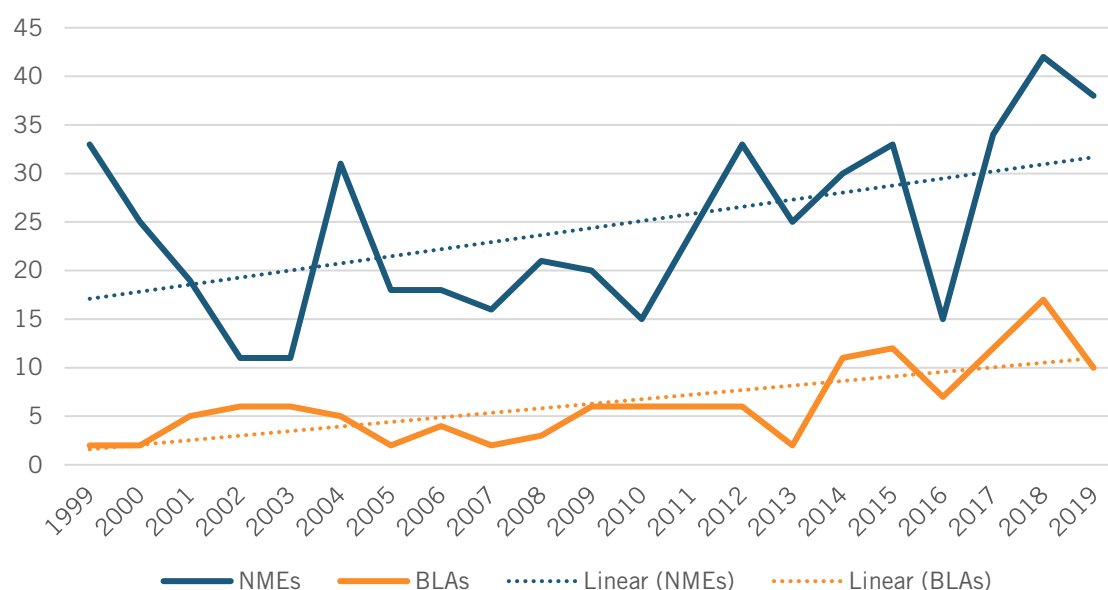


## New Drugs

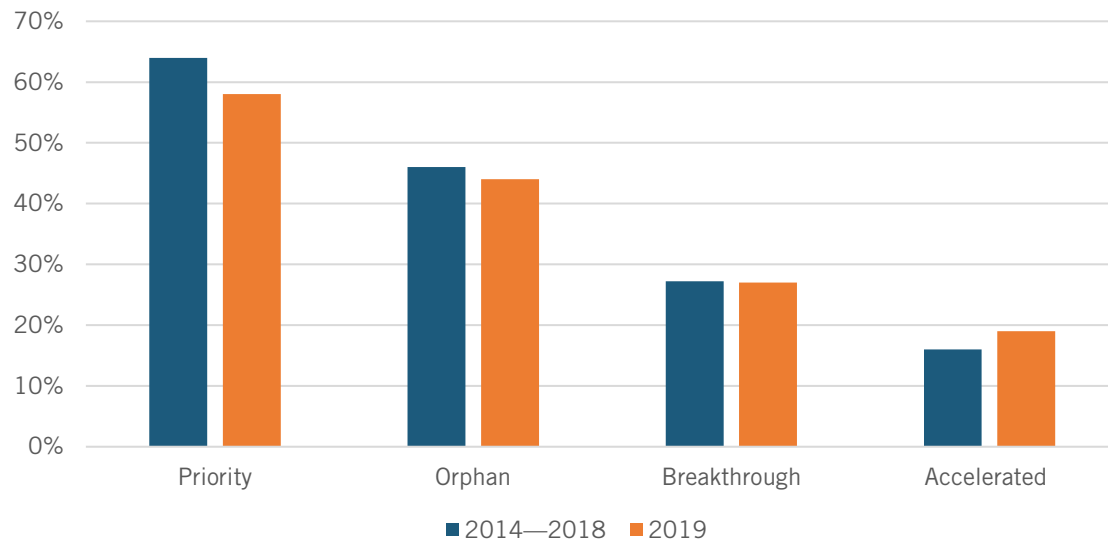
The pace of biomedical innovation has grown over the past two decades. The FDA CDER's 5-year rolling approval average stands at 44 new drugs per year, double the lowest 5-year rolling average, of 22 drugs approved, realized in 2009. (See figure 9.) The trend lines for both non-molecular entities (NMEs) and biologics license applications (BLAs) are rising.

In 2019, cancer remained the dominant therapeutic area, accounting for 11, or 23 percent, of drug approvals (in line with a 25 percent average over the past 5 years), followed by neurological drugs, with 9, or 19 percent, of approvals, and non-cancer hematology products, with 13 percent of approvals.<sup>55</sup>

**Figure 9: FDA annual approvals of NMEs and BLAs, 1999–2019<sup>56</sup>**



**Figure 10: Drug approvals by regulatory designation, 2014–2019<sup>57</sup>**



In 2019, 28 CDER-approved drugs (58 percent) were of priority review products, for therapies expected to offer significant improvement over existing products, while 13 (or 27 percent) of the drugs approved were breakthrough designees, as they likewise represent substantial improvements over existing drugs (these categories are not mutually exclusive). (See figure 10.) Twenty-one, or 44 percent, of the drugs approved treat rare diseases, those that afflict fewer than 200,000 patients, while 19 percent of products received accelerated approval on the basis of improvements in surrogate endpoints rather than clinical ones.<sup>58</sup> In 2018, personalized medicines accounted for 42 percent of new medicines approved by the FDA, a sharp increase from 2005, when just 5 percent were personalized medicines.<sup>59</sup> (Figure 10 also compares the 2019 figures with the 2014 to 2018 average.) Taken together, these numbers show how the PDUFA has stimulated biopharmaceutical innovation by creating new regulatory-approval pathways such as the breakthrough designation.

### Trade Performance

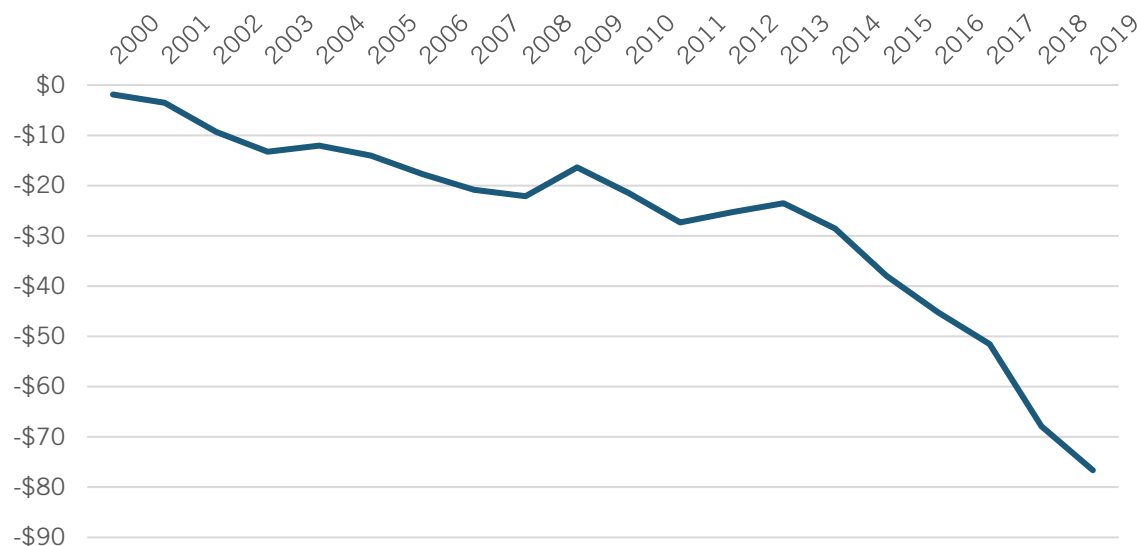
The nominal value of U.S. biopharmaceutical exports increased 35 percent from 2010 (\$49.4 billion) to 2019 (\$66.7 billion). However, U.S. GDP increased 48 percent over this time. To have kept pace with the growth of GDP, exports would have had to increase to \$73 billion. Over the same period, imports grew from \$87 billion to \$152 billion, a 75 percent increase.<sup>60</sup>

This is one reason why the U.S. trade deficit in the sector has significantly worsened over the past decade, more than quadrupling from a deficit of \$16 billion in 2010 to \$77 billion in 2019. In 2000, the trade deficit in the sector was just \$2 billion. (See figure 11.)

The U.S. trade balance in pharmaceuticals with peer nations has steadily worsened since 1991. (See table 1.) There are a number of likely reasons for this poor trade performance. Low wages are a main driver in the case of India, but don't provide an explanation for the sizeable trade deficits with nations such as Germany, Switzerland, and Ireland. In 2016, average manufacturing labor costs in dollar terms were 55 percent higher in Switzerland, 11 percent higher for Germany, and just 9 percent lower in Ireland.<sup>61</sup> In the case of Germany and Switzerland, the competitive strength of leading companies such as Bayer, Roche, and Novartis,

coupled with both nations having strong national manufacturing and engineering systems as well as financial systems that don't penalize companies for investing heavily in long-term capital intensive assets, likely explains much of the surplus.

**Figure 11: U.S. trade balance in pharmaceutical products and preparations<sup>62</sup>**



**Table 1: Trade balance in pharmaceuticals with the United States (in billions)<sup>63</sup>**

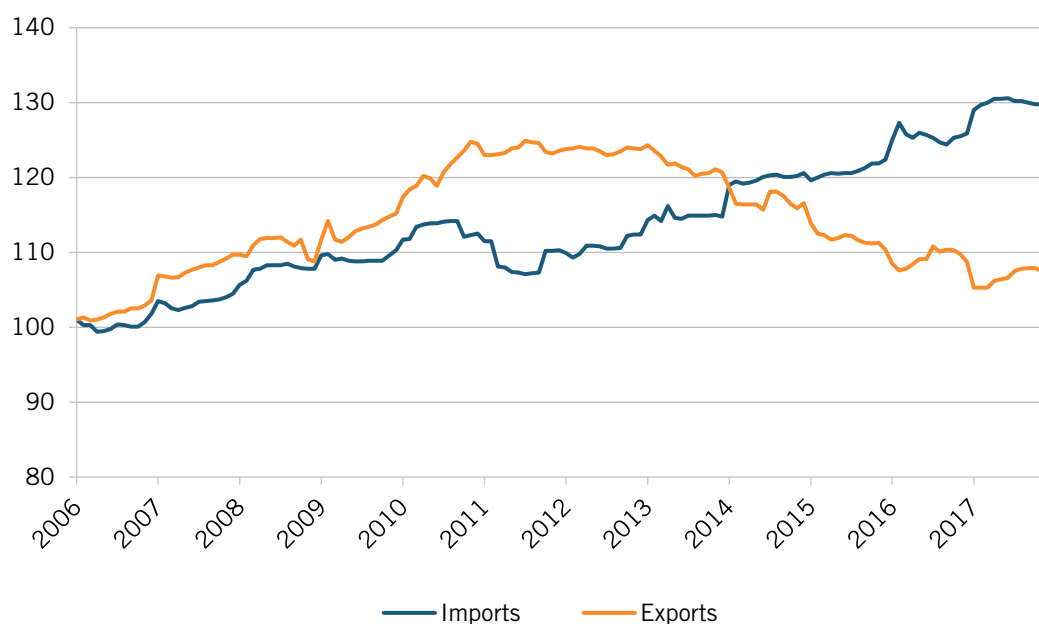
Country	1991	1996	2001	2006	2011	2016	2019
Canada	\$0.4	\$0.6	\$0.9	-\$0.2	\$1.0	-\$1.2	-\$1.0
China	\$0.0	\$0	\$0	-\$0.1	\$0.1	\$0.6	\$2.5
France	\$0	\$0	-\$0.8	-\$2.7	-\$2.3	-\$2.0	-\$2.4
Germany	\$0.1	\$0.1	-\$1.6	-\$4.8	-\$6.0	-\$10.6	-\$12.4
India	\$0	\$0	-\$0.1	-\$0.4	-\$3.2	-\$7.2	-\$7.4
Ireland	-\$0.1	-\$0.3	-\$1.7	-\$5.5	-\$13.6	-\$13.7	-\$23.7
Israel	\$0	-\$0.1	-\$0.5	-\$2.4	-\$5.5	-\$4.8	-\$2.0
Japan	\$0.4	\$0.3	-\$0.5	\$0.1	\$1.3	\$1.7	-\$0.4
Netherlands	\$0.1	\$0.1	\$0.4	\$3.8	\$2.4	\$2.9	\$1.2
Singapore	\$0	\$0	\$0	-\$2.4	-\$1.1	-\$1.2	-\$3.4
South Korea	\$0	\$0.1	\$0.1	\$0.2	\$0.6	-\$1.8	-\$1.0
Switzerland	-\$0.2	-\$0.4	-\$0.6	-\$0.4	-\$4.3	-\$8.2	-\$13.7
United Kingdom	-\$0.3	-\$0.6	-\$0.2	-\$1.3	\$0.6	-\$1.7	-\$2.0
Rest of World	\$0.7	\$0.9	\$1.1	-\$1.2	\$2.3	\$1.7	-\$9.0
United States	\$1.1	\$0.7	-\$3.5	-\$17.3	-\$27.8	-\$45.6	-\$74.7

In the case of Ireland, the deficit is largely caused by tax policy. The Irish corporate tax rate is just 12.5 percent (6.25 percent on revenue tied to a patent or intellectual property). Some



companies, including Salix Pharmaceuticals and Medtronic, moved their corporate headquarters to Ireland to take advantage of this low rate. Other countries “domiciled” their intellectual property abroad by transferring ownership to a foreign subsidiary.<sup>64</sup> Until the 2017 tax reform, the United States taxed the worldwide income of its companies at a high 35 percent marginal tax rate. The 2017 tax reform was supposed to remove much of this disparity. The reform bill lowered the statutory rate to 21 percent. It also inserted a new provision giving companies an even lower rate on income derived from exports of intellectual property developed in the United States.<sup>65</sup> However, the reform might have had the opposite effect, causing pharmaceutical imports from Ireland to grow.<sup>66</sup> The movement away from taxing worldwide income may be outweighing the effect of the lower statutory tax since U.S. countries no longer need to move their headquarters to avoid U.S. tax. The OECD Base Erosion Profit Shifting (BEPS) process is working to develop a common approach, including establishing a global minimum tax, which would address this challenge.<sup>67</sup>

**Figure 12: BEA import/export price indexes for pharmaceutical and medicine manufacturing (Dec. 2005 = 100)<sup>68</sup>**



However, some of the high trade deficit in pharmaceuticals is at least partially due to mismeasurement of the value of exports and imports. One reason for this is that most other nations impose significant price controls on pharmaceuticals, artificially reducing the value—but not the quantity—of exports, making the trade deficit look worse than it actually is. The Bureau of Economic Analysis generally bases its values of traded goods on the value declared by the shipper. A foreign country imposing price controls on drugs is likely to lead U.S. exporters to value the declared drugs at the lower, policy-constrained price. In contrast, a foreign manufacturer shipping a similar drug in the same quantities to the United States will be recorded at the higher U.S. price, resulting in an import/export imbalance. The divergent prices help explain roughly 40 percent of the U.S. pharmaceutical trade deficit in 2016. (See figure 12.) In other words, foreign price controls appear to inflate the actual trade deficit, making it look roughly two-thirds larger than it would be without price differences.

## INTERNATIONAL COMPARISONS

The United States remains the leader in drug discovery, ranking first in nearly all measures of innovation.<sup>69</sup> For example, the 2017 Biopharmaceutical Competitiveness and Investment Survey ranked the United States first among mature markets—improving slightly from its 2016 score, with 86.89 out of 100—followed by Switzerland, Germany, and the United Kingdom.<sup>70</sup> The United States scored higher than the average of its top-three competitors in each of the survey's five categories, in addition to recently being ranked as the top location for life-sciences jobs in the world.<sup>71</sup>

### Leading Firms

The United States accounts for 3 of the world's 5 largest biopharmaceutical companies (Johnson & Johnson, Pfizer, and Merck) and 9 of the 20 largest. (See table 2.) Moreover, all of these foreign firms have significant numbers of jobs in the United States. For example, GlaxoSmithKline employs approximately 10,000 workers in the United States.<sup>72</sup> Novartis employs approximately 15,000 workers, located its global R&D headquarters, and has its latest-generation cell and gene manufacturing facilities in the United States.

**Table 2: World's top-20 pharmaceutical companies by 2019 revenues<sup>73</sup>**

Company	Headquarters	2019 Revenues (Billions)
Johnson & Johnson	United States	\$82.1
Roche	Switzerland	\$63.5
Pfizer	United States	\$51.7
Novartis	Switzerland	\$47.4
Merck & Co.	United States	\$46.8
GlaxoSmithKline	United Kingdom	\$43.3
Sanofi	France	\$40.5
AbbVie	United States	\$33.3
Takeda	Japan	\$29.9
Bayer	Germany	\$26.6
Bristol Myers Squibb	United States	\$26.1
AstraZeneca	United Kingdom	\$23.6
Amgen	United States	\$23.4
Gilead Sciences	United States	\$22.4
Eli Lilly	United States	\$22.3
Boehringer Ingelheim	Germany	\$21.3
Novo Nordisk	Denmark	\$18.0
Teva Pharmaceutical Industries	Israel	\$16.9
Allergan	Ireland	\$16.1
Biogen	United States	\$14.4

## R&D Investment

The United States has been the world's largest global funder of biomedical R&D investment over the past two decades—considering all investments made by government, companies, foundations, and universities—a share that some analyses suggested reached as high as 70 to 80 percent over that period.<sup>74</sup>

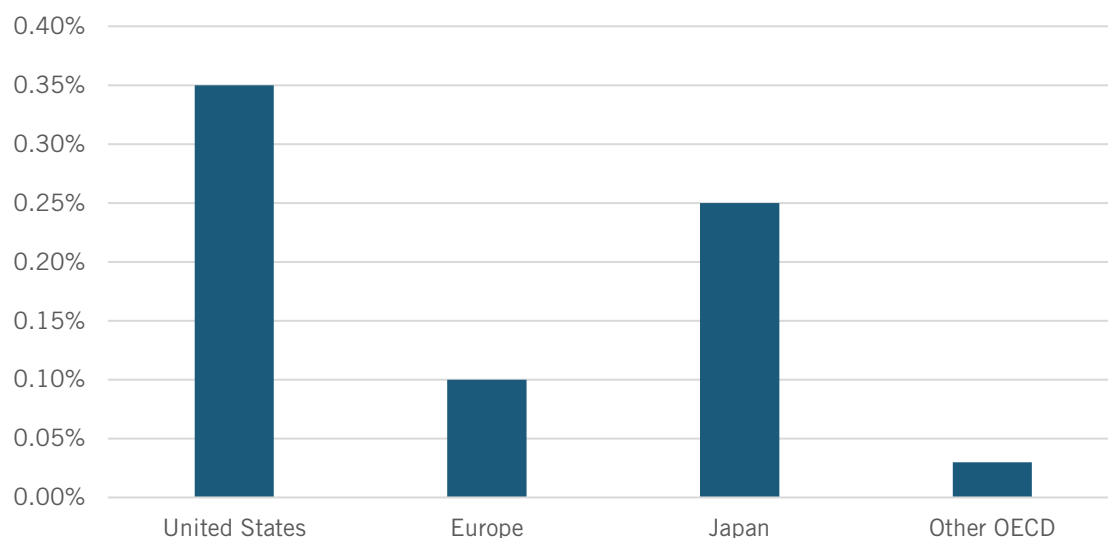
Considering enterprise R&D investment alone, companies in the United States invest far more in research than companies in other nations, and have increased their R&D investments by 20 percent since 2008. (See table 3.) Elsewhere, Chinese R&D grew over 300 percent from 2008 to 2017, while South Korea experienced 86 percent growth. In contrast, investment fell in Canada by 34 percent, in France by 24 percent, and in the United Kingdom by 6 percent.

**Table 3: Business enterprise R&D investment by industry, 2017<sup>75</sup>**

Country	Pharmaceuticals (Millions, in 2015 Dollars)	Increase Since 2008
Belgium	\$2,691	71%
Canada	\$394	-34%
China	\$14,699	307%
Denmark	\$1,309	34%
France	\$1,044	-24%
Germany	\$5,823	19%
Italy	\$789	12%
Japan	\$14,158	15%
South Korea	\$1,576	86%
United Kingdom	\$541	-6%
United States	\$63,966	20%

The United States also leads when investment in research is compared with GDP. Private investment in R&D in the United States amounted to 0.35 percent of GDP, compared with 0.25 percent for Japan, and 0.10 percent for Europe, meaning that as a share of GDP, U.S. companies invest more than three times the amount that European companies invest. (See figure 13.) Across the rest of the Organization for Economic Cooperation and Development (OECD), private enterprise invests 0.03 percent of GDP on pharmaceutical R&D.

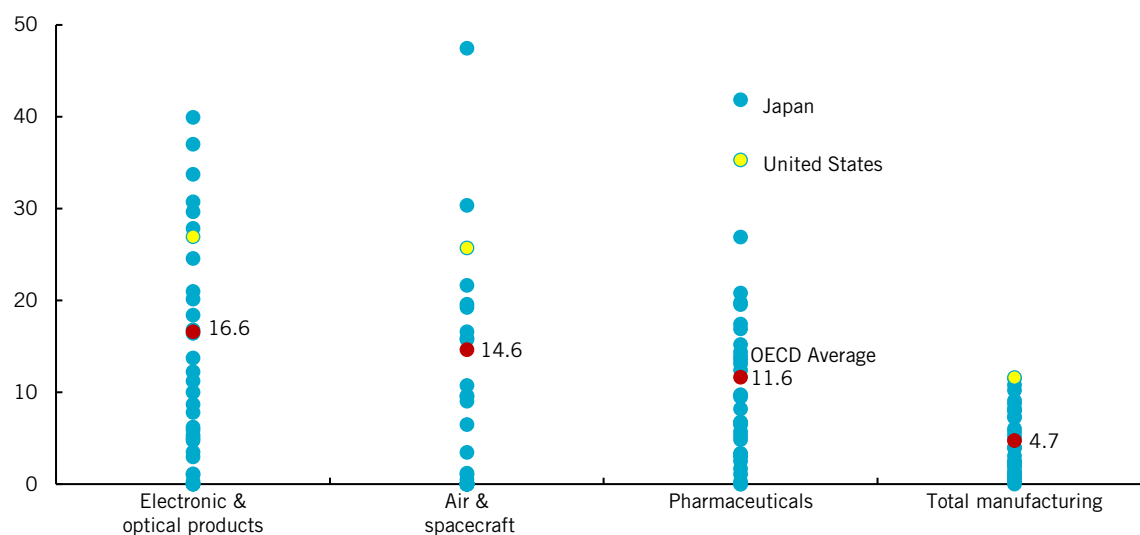
**Figure 13: Business investment in pharmaceutical R&D in 2016 as a percentage of GDP<sup>76</sup>**



**As a share of GDP, U.S. pharmaceutical companies invest more than three times the amount in R&D than their European peers do.**

A better way of considering private research contributions is as a percentage of the gross value added created by each industry. On this metric, U.S. pharmaceutical companies rank extremely well. In 2014, the latest year for which data is available, the U.S. pharmaceutical industry reinvested 32.3 percent of its total value added back into research. (See figure 14.) This was a higher percentage than for any other U.S. industry. Among other countries, it was surpassed only by Japan, which invested 41.8 percent of value added on R&D. Across OECD, the industry invests nearly 12 percent of its gross value added on R&D.

**Figure 14: Business enterprise R&D expenditure as a portion of gross value added<sup>77</sup>**



Likewise, when considered on an individual company level, U.S.-headquartered firms generally lead their international peers in R&D intensity (R&D investment as a percentage of sales). U.S.-based biopharmaceutical companies consistently led in R&D intensity in “The 2019 EU Industrial R&D Investment Scoreboard.” (See table 4.) Of the top-25 leading biopharma R&D investors in the study, 7 of the top-10 with the greatest R&D intensity hailed from the United States. And while certainly relatively smaller firms such as Incyte and Vertex can have much-greater R&D intensities, the trend follows for even the larger firms such as Celgene, Bristol Myers Squibb, and Merck. On average, of the top-25 biopharmaceutical R&D-investing companies in the study, American firms averaged an R&D intensity of 25.2 percent, Japanese firms 18.1 percent, and European firms 15.5 percent.<sup>78</sup> In terms of aggregate amounts, among the top-25 biopharmaceutical R&D investors, American firms accounted for €53.5 billion of R&D investment, European firms €47.9 billion, and Japanese firms €6.24 billion.

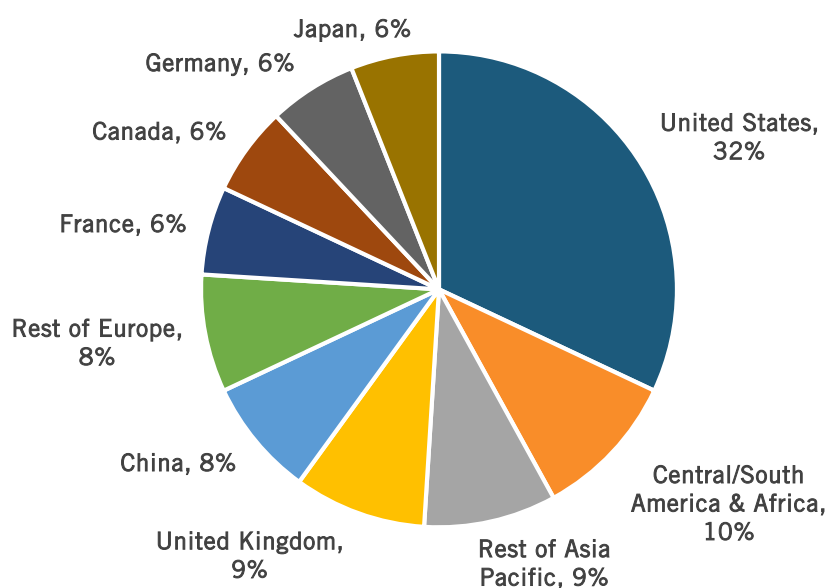
**Table 4: Leading biopharmaceutical investors on the 2019 EU Industrial R&D Investment Scoreboard<sup>79</sup>**

Company	Headquarters	R&D Investment (Billions of Euros)	R&D Intensity (%)
Incyte	United States	1.0	62.6
Vertex Pharma	United States	1.2	46.2
Celgene	United States	4.0	29.8
Bristol Myers Squibb	United States	5.5	27.8
AstraZeneca	United Kingdom	4.6	24.0
Merck US	United States	8.5	22.9
Daiichi Sankyo	Japan	1.6	21.9
Roche	Switzerland	9.8	19.4
Biogen	United States	2.3	19.3
Gilead Sciences	United States	3.7	19.0
Takeda	Japan	2.9	17.6
Novartis	Switzerland	8.0	17.2
Sanofi	France	5.9	17.1
Otsuka	Japan	1.7	16.7
AbbVie	United States	4.6	16.0
Astellas Pharma	Japan/United States	1.6	16.0
Amgen	United States	3.3	15.7
Eli Lilly	United States	3.2	15.0
Merck DE	Denmark	2.2	15.0
Pfizer	United States	6.8	14.5
Allergan	Ireland	2.0	14.3
Johnson & Johnson	United States	9.4	13.2
Bayer	Germany	5.1	12.9

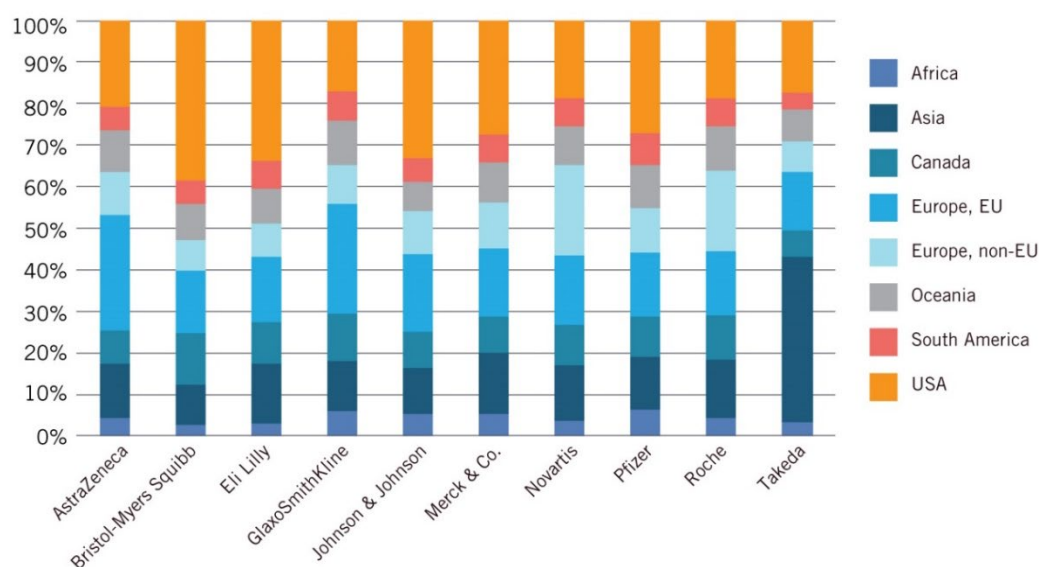
## R&D Performance

The location of the R&D activity is as important as the extent of nations' and enterprises' R&D investment. To begin with, the United States leads the world in both overall clinical trial activity, a global market valued at \$47 billion in 2019, as well as early-stage clinical research.<sup>80</sup> Almost one-third of global biopharmaceutical R&D activity occurs within the United States. (See figure 15.) Similarly, the world's leading life-sciences companies conduct the bulk of their life-sciences R&D activity in the United States. (See figure 16.)

**Figure 15: Where global biopharmaceutical R&D is occurring<sup>81</sup>**



**Figure 16: Countries where "Top-10" life-sciences R&D companies are conducting their R&D activity<sup>82</sup>**

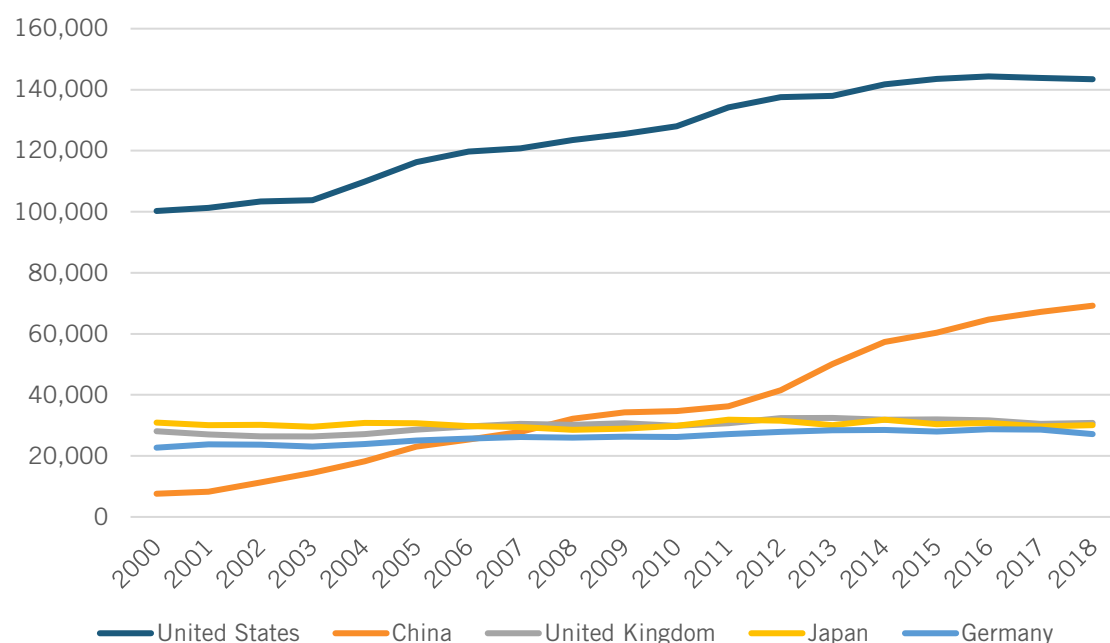


However, this strong performance in R&D and innovation should not be cause for complacency. As the U.S International Trade Administration wrote: “Conditions that limited R&D offshoring in the past, such as market proximity and availability of talent, are rapidly shifting. The pharmaceutical sector is often targeted by protectionist or industrial policies as governments around the world view it as strategically import.”<sup>83</sup>

## Scientific Publications

The five leading nations for scientific publications in the health sciences as of 2018 were the United States, China, the United Kingdom, Japan, and Germany. The United States produced over 140,000 such publications in 2018, up 40 percent from about 100,000 in 2000. Health sciences publications held constant in most other nations, but China’s increased over nine-fold, from 7,600 to almost 70,000. (See figure 17.)

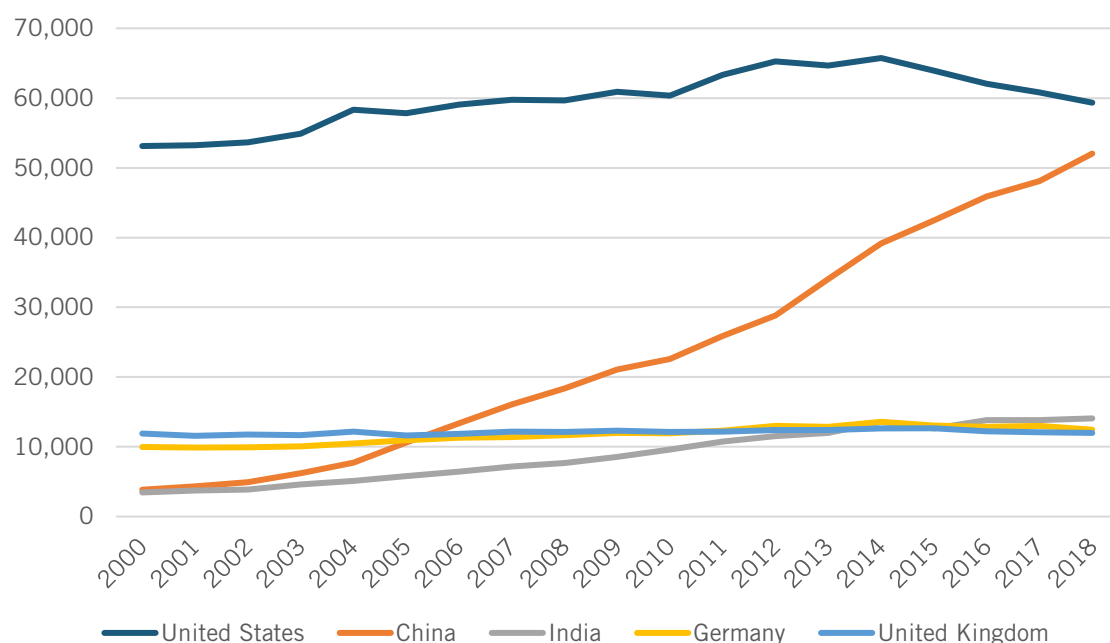
**Figure 17: Countries’ health sciences scientific publications<sup>84</sup>**



U.S. biology and biomedicine scientific publications increased overall from 2000 to 2018, but, troublingly, decreased from 2014 to 2018. (See figure 18.) China’s biology and biomedicine scientific publications increased from 6,200 in 2000 to over 52,000 in 2018, an eight-fold increase. Germany’s and the United Kingdom’s publication levels remained mostly level, although India’s more than doubled over this time.



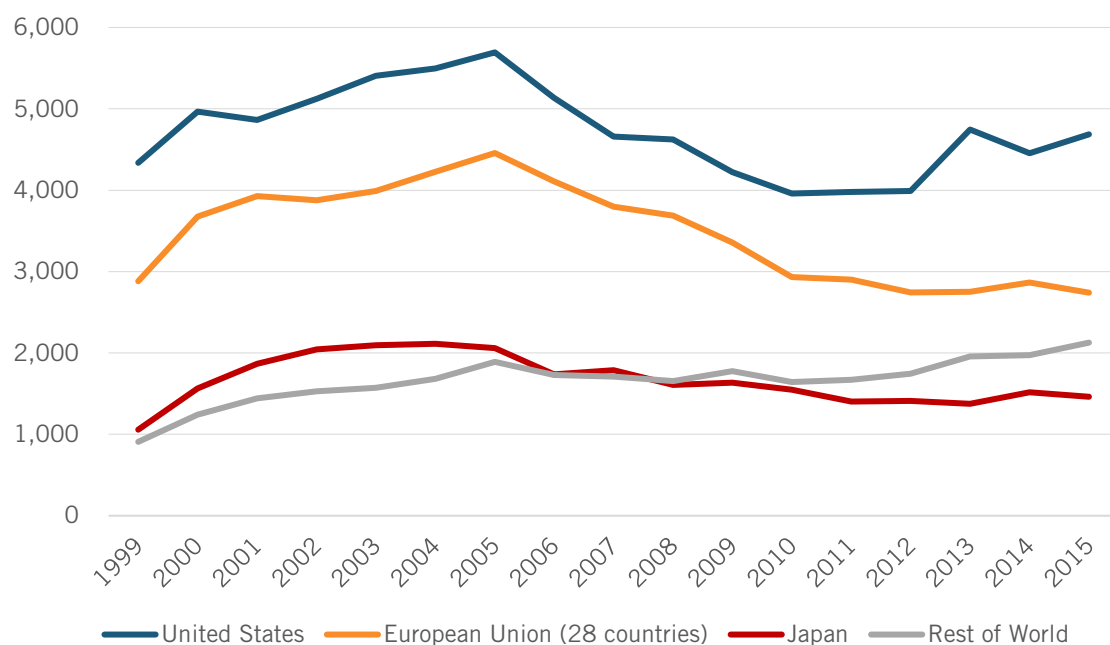
**Figure 18: Countries' biology and biomedicine scientific publications<sup>85</sup>**



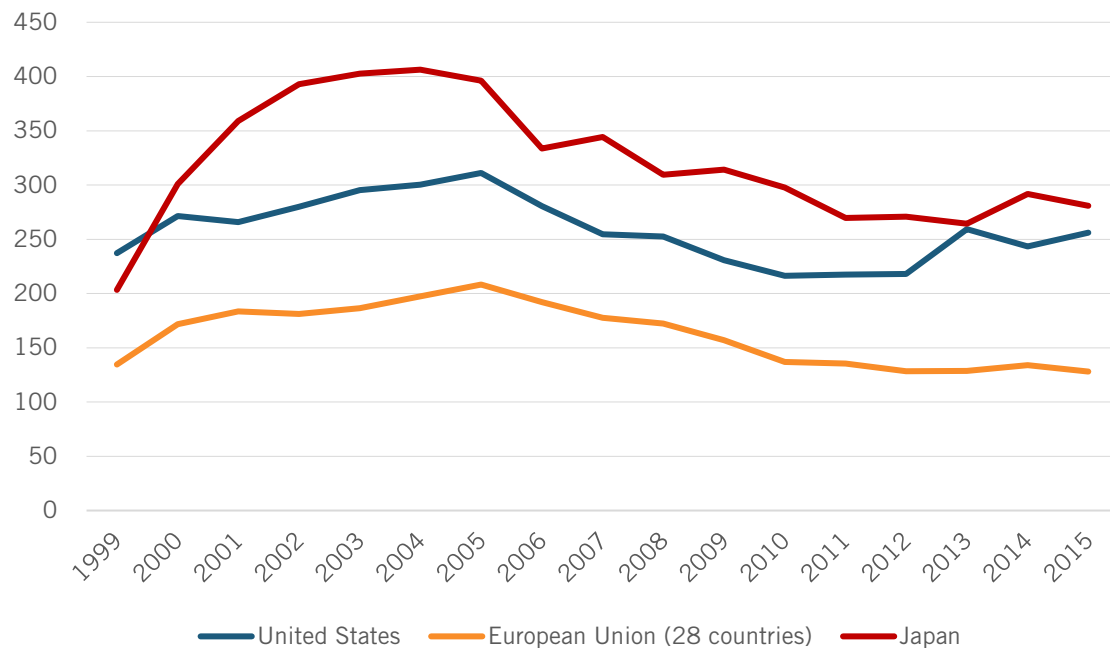
## Patents

The OECD provides internationally comparable data on triadic patents, which refer to a series of corresponding patents filed simultaneously at the European, Japanese, and U.S. patent offices. The United States leads Europe, Japan, China, and other nations combined in terms of triadic biotechnology and pharmaceutical patent applications. U.S. filings increased by several hundred annually from 1999 to 2015; however, they dipped from a high of 5,694 in 2005 to 4,688 in 2015, the latest year for which this data is available. (See figure 19.)

**Figure 19: Number of triadic biotechnology and pharmaceuticals patent applications by priority date<sup>86</sup>**



**Figure 20: Number of triadic biotechnology and pharmaceuticals patent applications per trillion of U.S. GDP in 2019<sup>87</sup>**



Japan's filings of triadic biotechnology and pharmaceutical patent applications increased by 40 percent from 2009 to 2015. Moreover, Japan actually leads the United States when the number of triadic biotechnology and pharmaceutical patent applications are considered as a share of GDP, with the country producing almost twice as many patents as European Union countries as a share of GDP. (See figure 20.) What is particularly striking—though not unexpected given their policies—is the EU's poor performance, including on drug pricing.

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**From 2004 to 2018, U.S.-headquartered enterprises produced almost twice as many new drugs as did European ones, and three to four times as many as Japan, or all other nations combined.**

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### New Drugs

The acid test of nations' and enterprises' investments in R&D and scientific publications is whether this effort actually translates into the introduction of new-to-the-world drugs. On this score, again, the United States excels, and its lead is growing. According to data provided by the European Federation of Pharmaceutical Industries and Associations, from 2004 to 2018, U.S.-headquartered enterprises produced almost twice as many new chemical or biological entities (NCEs and NBEs) as did European ones, and three to four times as many as Japan, or all other nations combined. (See table 5.) From 2009 to 2018, U.S.-headquartered companies outstripped European ones with 189 to 133 new NCEs and NBEs (and Japan and all other countries 189 to 111). Note that this growth is part of an even longer-term trend; between 1975 and 1979, Europe led the United States, with 149 drugs to 66.<sup>88</sup> When considering new drugs as a share of GDP, the United States also leads, but not by as much, followed by Japan and Europe (See table 6.)

**Table 5: Number of new chemical or biological entities<sup>89</sup>**

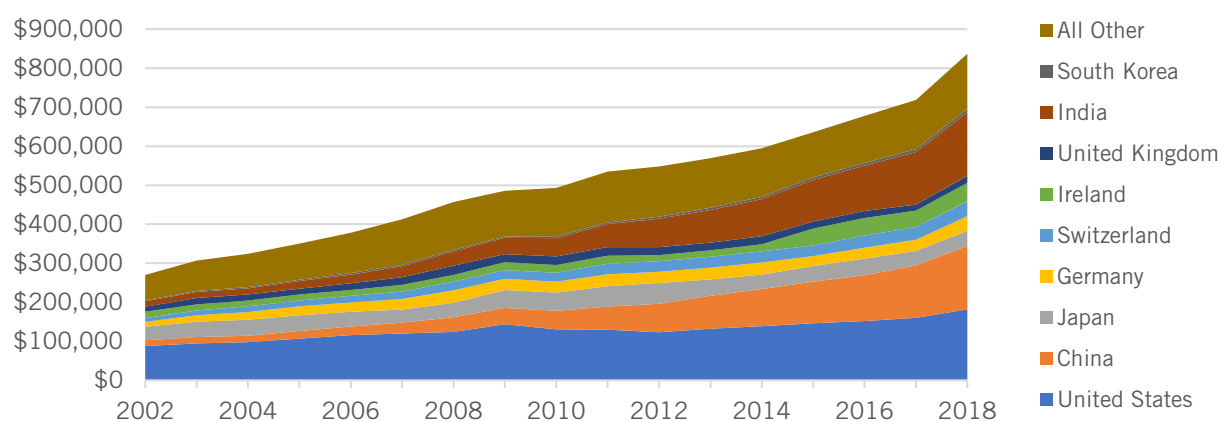
Region	1999–2003	2004–2008	2009–2013	2014–2018	Total: 2009–2018
Europe	62	47	66	67	133
U.S.	73	67	64	125	189
Japan	28	16	26	34	50
Other	8	14	23	41	64

**Table 6: Number of new chemical or biological entities, per \$ trillion<sup>90</sup>**

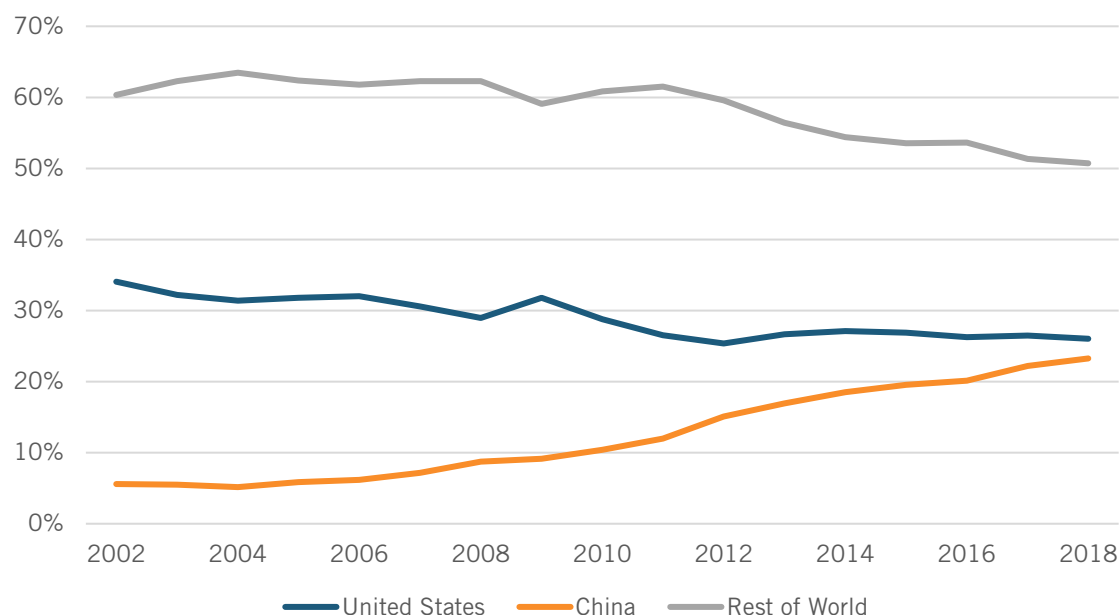
Region	1999–2003	2004–2008	2009–2013	2014–2018	Total: 2009–2018
Europe	1.53	0.70	0.88	0.91	0.90
U.S.	1.38	0.98	0.82	1.32	1.10
Japan	1.25	0.68	0.91	1.42	0.95
Other	0.14	0.13	0.13	0.20	0.17

### Value Added and Trade Performance

The U.S. pharmaceutical industry produced \$181.8 billion of value added in 2018, up 107 percent from the \$88 billion it produced in 2002. However, global value added increased much more, at 170 percent. Some of that increase globally reflected the growth of domestic markets and resultant local production in developing nations. For example, Chinese output grew by more than 10 times, while Indian value added grew by 7 times. (See figure 21.) As a result, China now ranks third behind the European Union and the United States in biopharma production. But some of this increase was in mature regions where markets were not growing, but production was. For example, value added doubled in Germany and almost tripled in Switzerland. As a result of this increased international competition, the United States' share of the world total of global pharmaceutical industry value added fell from 34 to 26 percent from 2002 to 2018, while China's grew over four-fold from 5.6 to 23 percent. (See figure 22.)

**Figure 21: Global value added of pharmaceutical industry (millions)<sup>91</sup>**

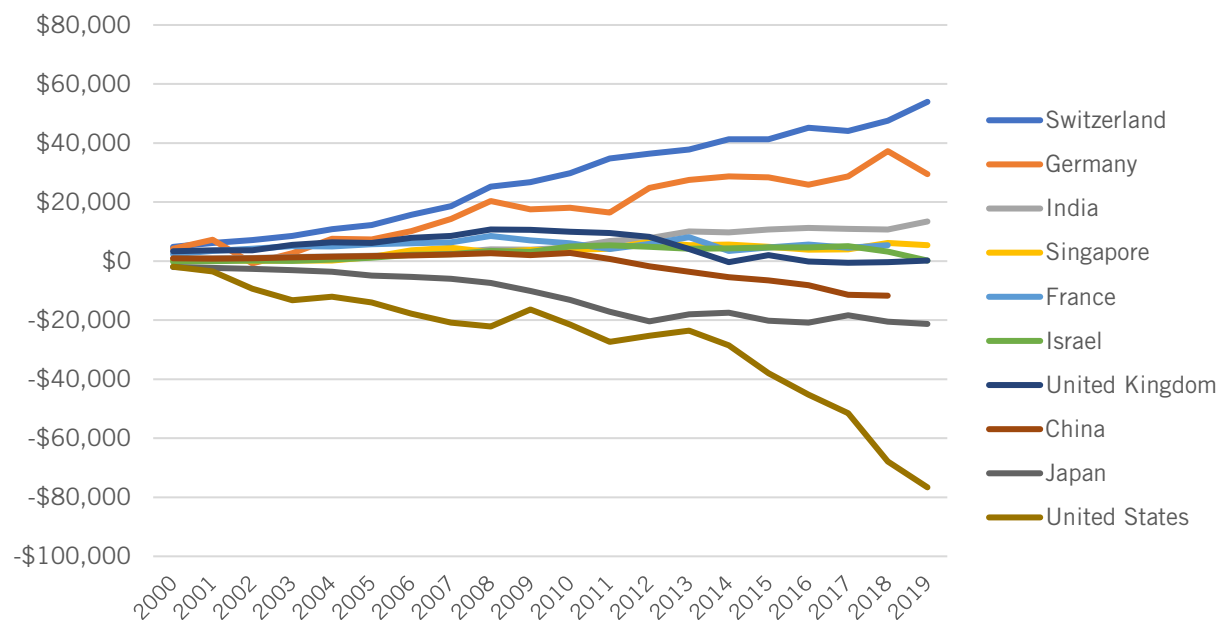
**Figure 22: Shares of value added in global pharmaceutical industry, by select country<sup>92</sup>**



### Trade Performance

As discussed, the United States has been running growing trade deficits in pharmaceutical products since 2001, but the increase accelerated after 2009 and has carried through to 2019. The U.S. trade deficit in pharmaceutical products significantly worsened over this period. Japan also runs trade deficits. Switzerland and, to a lesser extent, Germany, India, and Singapore have seen growing trade surpluses in the sector. (See figure 23.)

**Figure 23: Trade balance in pharmaceutical products and preparations, 2000–2019 (in millions)<sup>93</sup>**



## THE U.S. POLICY SYSTEM

There is a phrase that many advocates of stronger U.S. competitiveness use: “Invent and make in America.”<sup>94</sup> In other words, while global leadership in the innovation part of the production process is critical, nations also need at least reasonable strengths in manufacturing, especially the manufacturing of complex drugs.

The United States was once a global also-ran in biomedical innovation, but it’s become the world leader thanks to the adoption of a broad set of public policies including increases in public investment in biomedical research; effective technology transfer and commercialization mechanisms; robust IP protections; a pricing system that allows innovators to earn sufficient revenues to reinvest in innovation; tax incentives to encourage investment; and an effective drug approval system.

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**A signature strength of America’s biopharmaceutical innovation system has been complementarity between public and private-sector investment in life-sciences R&D.**

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### Complementary, and Robust, Public and Private-Sector R&D Investment

A signature strength of America’s biopharmaceutical innovation system has been the complementarity between public and private-sector investment in life-sciences R&D. The federal government, principally through NIH, funds basic research in the life sciences that sets the stage for the industry-led basic and applied R&D activity. That activity leads to the commercialization of new medicines and treatments.<sup>95</sup> NIH-funded basic life-sciences research—for instance, into understanding the fundamental processes by which diseases develop and are transmitted, or identifying novel biomarkers that signal the presence of a disease—creates a platform for innovation that has led not only to the discovery of new medicines, but to new tests (e.g., blood tests for substances), new procedures (e.g., improved cardiac stents that substitute for surgery), and new equipment (e.g., gene sequencers).<sup>96</sup> NIH’s FY 2019 funding of \$39.3 billion has been increased to \$41.69 billion for FY 2020 (although this includes an additional \$3.59 billion for three coronavirus-related emergency supplemental appropriations).<sup>97</sup>

Whereas public-sector researchers have performed the upstream, earlier-stage research elucidating the underlying mechanisms of disease and identifying promising points of intervention, business researchers perform basic research as well as the downstream, applied research resulting in the discovery of drugs for the treatment of diseases, in addition to carrying out the development activities necessary to bring new drugs to market.<sup>98</sup> In essence, while the federal government primarily funds basic scientific research, private-sector companies perform much of the applied R&D, including the completion of clinical trials required to transform basic scientific research into commercial products.

As a 2000 U.S. Senate Joint Economic Committee summarized the dynamic, “Federal research and private research in medicine are complementary. As medical knowledge grows, federal research and private research are becoming more intertwined, building the networks of knowledge that are important for generating new discoveries and applications.”<sup>99</sup> Similarly, as DiMasi, Milne, Cotter, and Chakravarthy concluded from a 2016 study of the roles of the private and public sectors in drug development, “Industry’s contributions to the R&D of innovative drugs go beyond development and marketing and include basic and applied science, discovery

technologies, and manufacturing protocols,” and that “without private investment in the applied sciences there would be no return on public investment in basic science.”<sup>100</sup>

These “spillovers” effectively provide firms with a common platform of basic knowledge, and thus induce greater levels of innovation. For the life-sciences industry, Dr. Everett Ehrlich found that a dollar of NIH support for research leads to an increase of private medical research of roughly 32 cents.<sup>101</sup> Similar findings were reported in a 2012 Milken Institute study, which finds that \$1 of NIH funding boosted the size of the bioscience industry by \$1.70, and that the long-term impact may be as high as \$3.20 for every dollar spent.<sup>102</sup> Likewise, a 2013 report by Battelle found that, looking solely at federal support for the Human Genome Project between 1988 and 2012, every dollar of federal funding helped generate an additional \$65 in genetics-related private activity.<sup>103</sup> Rutgers University Professor A.A. Toole identified a quantifiable correlation between investment in publicly funded basic research and corporate-funded applied research wherein an increase of 1 percent in the funding of public basic research led to an increase of 1.8 percent in the number of successful applications for new molecular entities after a lag of about 17 years. Toole concluded that a \$1 investment in public-sector basic research yielded \$0.43 in annual benefits in the development of new molecular entities in perpetuity—a remarkable return on investment.<sup>104</sup> Similarly, Lichtenberg estimated a social return from pharmaceutical innovation of 67.5 percent.<sup>105</sup> The total social return from biomedical research (public and private) has been estimated at 150 percent, implying that society would benefit from a significant increase in research spending (which, ironically, is the opposite of what would likely happen if widespread restrictions on drug prices were imposed).<sup>106</sup>

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**One study found that biotechnology companies invest \$100 in development for every \$1 the government invests in research that leads to an innovation.**

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However, the increasingly popular view in policy circles today that public funding of research underwrites the research and development of many prescription drugs is simply wrong. Proponents of “drug populism” make this claim to justify demands for lower drug prices or weaker intellectual property protections. But it’s critical to remember that significant investment is required to bring a drug to market even after considerable amounts of basic research have been conducted. In fact, one study found that biotechnology companies invest \$100 in development for every \$1 the government invests in research that leads to an innovation.<sup>107</sup> This highlights a critical point: it’s private companies, not the government or universities, that assume the risk of failure in trying to bring often-billion dollar projects over the finish line of Phase III clinical trials. That’s a key reason why separating the cost of biopharmaceutical R&D from the final market price of medicines would misalign incentives, raise bureaucratic costs, and limit innovation.<sup>108</sup>

## **Effective Technology Commercialization Policies**

Robust federal investment in basic life-sciences research would mean little without mechanisms to connect it with commercialization activity by the private sector. Unfortunately, for many decades, this was precisely the case, as federally funded life-science research sat on the shelves of universities, government research institutions, and national laboratories. In fact, when in 1968 President Lyndon Johnson asked his comptroller general, Elmer Staats, to assess how many drugs had been developed from NIH-funded research, Johnson was stunned to learn that

“not a single drug had been developed when patents were taken from universities [by the federal government].”<sup>109</sup> In fact, as late as 1978, the federal government had licensed less than 5 percent of the as many as 30,000 patents it owned.<sup>110</sup>

Recognizing that the federal government had a very weak track record of achieving commercialization of the research it funded, in 1980, Congress, on a bipartisan basis, introduced the Bayh-Dole Act, which confers to universities and nonprofit research institutions (such as the Battelle Memorial Institute, Sloan Kettering, and Massachusetts General Hospital) rights to the IP they generate from federally funded research.<sup>111</sup> Hailed by *The Economist* as “possibly the most inspired piece of legislation to be enacted in America over the past half-century” the Bayh-Dole Act has had a profound and lasting impact, especially by empowering universities to become key intermediaries and enablers of the U.S. innovation system.<sup>112</sup> For instance, while only 55 U.S. universities had been granted a patent in 1976, by 2006, 240 universities had been issued at least 1 patent.<sup>113</sup> And in just the first two decades after Bayh-Dole’s introduction (i.e., 1980 to 2002), American universities experienced a ten-fold increase in their patents and created more than 2,200 companies to exploit their technology.<sup>114</sup> In other words, Bayh-Dole has played a key catalytic role in turning U.S. universities into engines of innovation. In total, from 1996 to 2017, licensing of technologies from universities to the private sector contributed to 420,000 invention disclosures, 100,000 patents issued, and the formation of 13,000 start-up companies.<sup>115</sup> As of May 2020, a very “back-of-the envelope” calculation found a 35 percent licensed innovation rate stemming from university-conducted, largely federally funded research.<sup>116</sup>

In the life-sciences sector in particular, Bayh-Dole has transformed U.S. universities into key developers of and conduits for novel IP stemming from federally funded research. In 2017, U.S. universities conducted \$68.2 billion in research activity, with \$39.8 billion funded by federal sources; \$23.6 billion contributed by “other” sources, including universities themselves and other nonprofit research institutions; and \$4.8 billion contributed by industry.<sup>117</sup> Bayh-Dole enables universities to retain the IP rights stemming from federally funded, university-conducted basic life-sciences research, which universities then often license to businesses (with 67 percent of these university licenses going to start-ups and small businesses) or research institutes, so that this novel IP can be commercialized into innovative drugs or therapeutics. It’s largely through this process that the public-private partnerships the Bayh-Dole Act catalyzed have led to the development of over 300 novel drugs and vaccines.<sup>118</sup> These medicines treat conditions ranging from Crohn’s disease to hepatitis B, HIV/AIDS, and HPV, melanoma, CML, and inherited blindness.<sup>119</sup>

The Bayh-Dole Act has also proven pivotal in facilitating the development of tests, treatments, and vaccines combatting the coronavirus. For instance, Moderna, the company that has come the furthest in developing a coronavirus vaccine—with Phase II clinical trials already underway in Seattle—credits the pivotal role of patents in the fields of messenger RNA and associated mRNA delivery technologies, which it licensed from Harvard and the University of Pennsylvania.<sup>120</sup> Similarly, Ridgeback Biotherapeutics, which is developing the only oral direct-acting antiviral vaccine treatment for the coronavirus, licensed key COVID-19 technology from Emory University. Gilead Sciences partnered with various universities, led by the University of Alabama, on its remdesivir research dating back to 2014.<sup>121</sup> Another company, Cepheid, which has developed a point-of-care COVID-19 diagnostic, leveraged Bayh-Dole to license technology developed at the



Lawrence Livermore National Laboratory for technology for rapid polymerase chain reaction thermocycling, integrating amplification, and detection.<sup>122</sup> There are dozens more examples, but in short the Bayh-Dole Act has and continues to play a foundational role in enabling the government-academic-industry partnerships so critical to U.S. life-sciences leadership.

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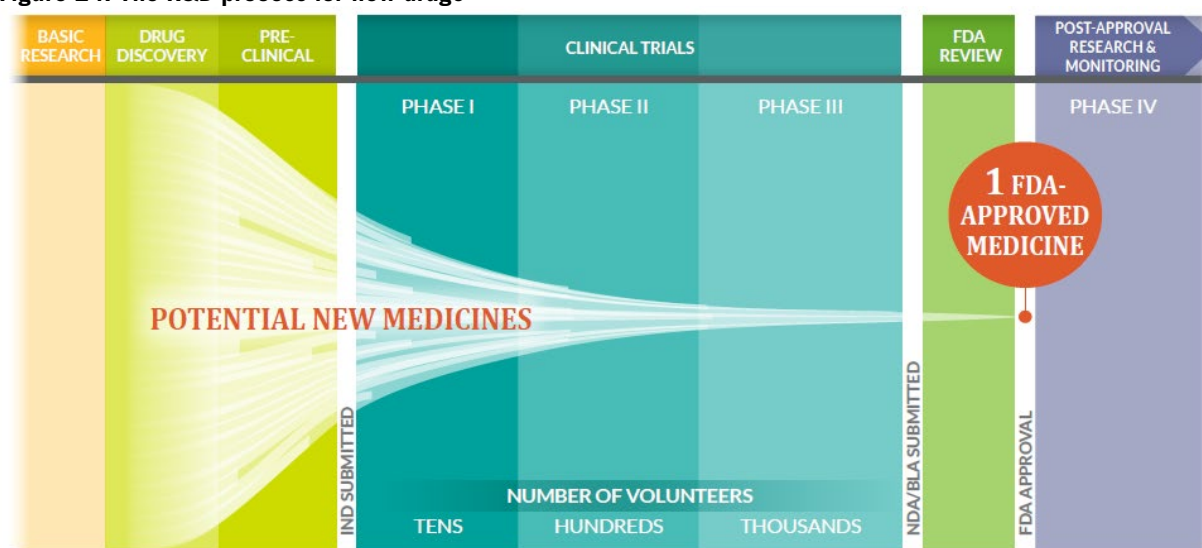
**Robust federal investment in basic life-sciences research would mean little without mechanisms to connect it with commercialization activity by the private sector.**

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## A Drug Pricing System Enabling Companies to Recoup and Reinvest Profits to Innovate

The biopharmaceutical industry must be R&D intensive because bringing innovative new drugs to market represents a risky, time-consuming, and expensive process. The stages involved in bringing a new drug to market begin with basic research, drug discovery, and preclinical trials; then proceed to three stages of human clinical trials, which culminate in a drug's approval (or rejection) by the FDA; and finally culminate in pharmacovigilance (that is, post-approval safety monitoring). (See figure 24.) Biopharmaceutical companies conduct laboratory screening of 5,000 to 10,000 chemical compounds for each new drug approved for use in humans. On average, as many as 5,000 to 10,000 compounds may be screened to get to approximately 250 promising molecular compounds that can enter preclinical testing, with 5 entering actual clinical testing.<sup>123</sup> And that's just getting to the clinical trial stage, as less than 12 percent of candidate medicines that even make it into Phase I clinical trials are ultimately approved by the FDA.<sup>124</sup>

**Figure 24: The R&D process for new drugs<sup>125</sup>**



Key: IND=Investigational New Drug Application, NDA=New Drug Application, BLA=Biologics License Application

The drug development process has grown increasingly expensive. For instance, according to a 2018 report “Unlocking R&D Productivity: Measuring the Return From Pharmaceutical Innovation 2018” by the Deloitte Center for Health Solutions, “The average cost to develop an asset, including the cost of failure, has increased in six out of eight years.”<sup>126</sup> The report estimates that the cost of developing a new drug almost doubled from an average cost of \$1.19 billion in 2010 to \$2.17 billion in 2018. The 2019 version of the report concludes that the average cost of bringing a new drug to market has increased by 67 percent since 2010 alone.<sup>127</sup>

An in-depth study conducted by the Tufts University Center for the Study of Drug Discovery, “Cost of Developing a New Drug,” estimates that the average cost of developing a new drug in 2014 was \$2.56 billion.<sup>128</sup> While certainly numerous studies exist, they generally confirm the expensive and lengthy nature of new drug development, finding that developing new drugs requires an average of 11.5 to 15 years of research, development, and clinical trials, at a cost of \$1.7 billion to \$3.2 billion.<sup>129</sup>

Only a small fraction of drugs that enter clinical trial testing are ultimately approved by the FDA, and an even smaller fraction of approved drugs ever become economically profitable. A study released in 2010 by Vernon, Golec, and DiMasi found that 80 percent of new drugs made less than their capitalized R&D costs. Entities in the second-most-profitable decile barely broke even; and those in the first decile had discounted profits that were more than twice their discounted R&D costs.<sup>130</sup> Other studies have found that of the most successful 10 percent of approved drugs, only 1 percent of those that entered clinical trials—maybe 3 new drugs each year—generate half of the profits of the entire drug industry.<sup>131</sup>

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Just like any other innovation-based industry, U.S. life-sciences companies depend upon the profits earned from one generation of innovation to finance investment in the next, a dynamic especially vital in such a capital-intensive industry as biopharmaceuticals. The ability to earn profits from successful drugs is foundational to perpetuating that dynamic.

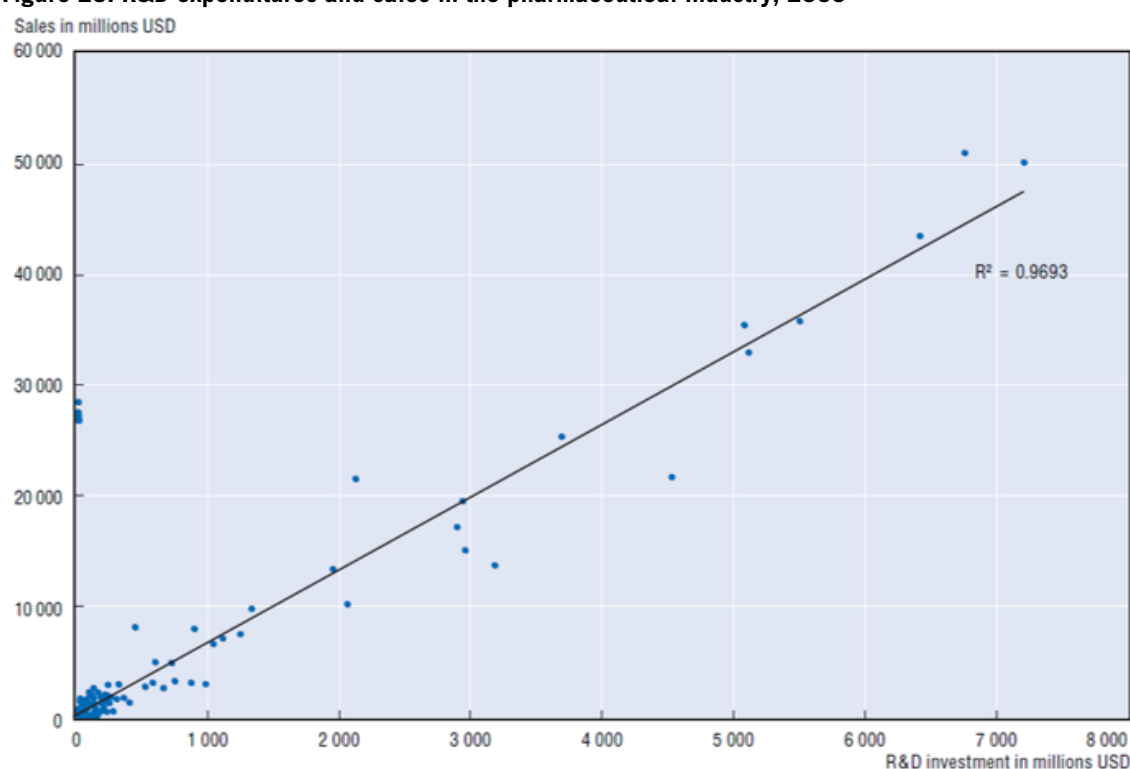
For instance, consider the history of successes and failures at Gilead Sciences, a company genuinely committed to breakthrough biomedical innovation. Among others, in 2012, it introduced Truvada, an HIV-prevention drug; in 2013, it introduced Sovaldi, the hepatitis C cure; and in 2020, it introduced remdesivir, the first FDA-sanctioned coronavirus therapeutic, derived from 2018 research it undertook in efforts to develop a treatment for the Ebola virus. Against this backdrop, Gilead’s gambit to tackle pancreatic cancer in 2014 (a gruesome disease for which there remains no treatment whatsoever) faltered when simtuzumab failed Phase I clinical trials; in 2016, Gilead’s momelotinib, a treatment for the bone-marrow disorder myelofibrosis, delivered disappointing Phase II clinical trials and was scrapped; and, in 2019, Gilead suffered a high-profile Phase III clinical trial failure when it pulled the plug on selonsertib as a possible treatment for liver disease. Critics skewered Gilead for charging what was thought to be too much for Sovaldi at the time, and they now want Gilead to price remdesivir at \$1 a dose (roughly its marginal cost). But the reality is Gilead represents a perfect case study of a life-sciences innovator leveraging the profits from one generation of innovations to reinvest in the next, perpetuating a virtuous cycle; so an HIV prevention drug and a hepatitis C treatment contribute (in knowledge and capital) to a coronavirus treatment, whose success hopefully begets resources that Gilead can redeploy when it tries again to tackle pancreatic cancer, or other similarly pernicious diseases.<sup>132</sup>

This pattern illustrates why there are extremely close linkages between the profits life-sciences companies earn and their ability to invest in future R&D. For instance, Dubois et al. found that every \$2.5 billion of additional revenue leads to a new drug approval.<sup>133</sup> As OECD plainly stated,

“There exists a high degree of correlation between pharmaceutical sales revenues and R&D expenditures.”<sup>134</sup> Indeed, there exists an almost 1:1 correlation (0.97) between R&D expenditures and sales. (See figure 25.)

Moreover, data from the United Kingdom’s Department of Innovation, Universities, and Skills R&D Scoreboard shows a very strong relationship between R&D and sales for the largest 151 pharmaceutical firms worldwide.<sup>135</sup> Similarly, Henderson and Cockburn have identified scale effects for R&D in the pharmaceutical industry, finding that R&D expenditures are directly proportional to the sales revenues available to undertake R&D investment.<sup>136</sup> This explains why academic research shows a statistically significant relationship between a biopharma enterprise’s profits from the previous year and its R&D expenditures in the current year.<sup>137</sup> Moreover, the pharmaceutical firms with the greatest sales are also the ones with the largest R&D investments, which may in part explain why most global R&D investments are undertaken by the largest multinational firms.<sup>138</sup> Symeonidis noted that this is in part because large firms are better able to spread the risks of R&D uncertainty, since they can undertake several projects simultaneously.<sup>139</sup> Likewise, Gambardella determined that sales revenue from previous periods have a significant, positive impact on current-period biopharma R&D.<sup>140</sup>

**Figure 25: R&D expenditures and sales in the pharmaceutical industry, 2006<sup>141</sup>**



Note: The data were prepared on the basis of annual reports and consolidated accounts received up to and including 31 July 2006. Annual reports with a year-end older than 30 months from the cut-off date or a publication date older than 24 months from cut-off date are excluded.

Source: DIUS (2007).

This dynamic further explains why a number of studies have found that reducing profits—such as through drug price controls, whether implemented through foreign drug reference pricing schemes or other directly imposed limits—would reduce R&D investment and therefore the number of new drugs innovated. For instance, Maloney and Civan found that a 50 percent drop

in U.S. drug prices would result in the number of drugs in the development pipeline decreasing by up to 24 percent.<sup>142</sup> Similarly, Golec and Vernon found that the United States using an EU-like drug pricing system from 1986–2004 would have resulted in a decline in firms' R&D expenditures of up to 33 percent and the development of 117 fewer new medicine compounds.<sup>143</sup> That research mirrored findings from a 2006 study by Zycher which found that while requiring federal negotiation of drug prices might decrease costs 35 percent from 2007 to 2025, doing so would lead to 196 fewer new medicines being developed, with a negative economic impact of \$500 million.<sup>144</sup>

More recently, in 2019, the Congressional Budget Office (CBO) examined the potential impact of the proposed House legislation H.R. 3, which among other provisions would require drug companies to negotiate lower prices with the government. CBO's preliminary conclusion was that reducing manufacturers' revenues by between \$500 billion and \$1 trillion over the next decade could result in 8 to 15 fewer new drugs coming to market over that time (out of about 300 that would otherwise be expected), reducing the number of new drugs by 3 to 5 percent over the ensuing decade.<sup>145</sup>

Conversely, research by Schwartz et al. found that if government price controls in non-U.S. OECD countries were lifted, the number of new treatments available would increase by 9 to 12 percent by 2030, equivalent to 8 to 13 new drugs in that year. This could potentially increase the life expectancy of someone 15 years old today by 0.6 to 1.6 years on average.<sup>146</sup> Analyses such as these explain why a February 2018 report by the president's Council of Economic Advisors found that while lowering reimbursement prices in the United States would reduce the prices Americans pay now for biopharmaceutical products, it would "make better health costlier in the future by curtailing innovation," thus failing to meet the administration's goal of reducing the price of health care by reducing the incentives for innovative products in the future.<sup>147</sup>

In 2018, CBO directly recognized the link between the expensive and risky process of drug development and the need to earn commensurate returns to sustain the process. CBO estimated that because of high failure rates, biopharmaceutical companies would need to earn a 61.8 percent rate of return on their successful new drug R&D projects in order to match a 4.8 percent after-tax rate of return on their investments (i.e., a risk-free rate they could readily attain in public markets).<sup>148</sup> The 61.8 percent figure is driven by two assumptions. The first is that 90 percent of new biopharmaceutical R&D projects fail, meaning all profits must come from the 10 percent that succeed. The second assumption in the CBO study was that it takes 12 years—during which companies spend large sums on development, testing, and approvals—for a successful project to start earning revenues. Concentrating only on the rate of return to successful projects therefore gives a misleading picture of the overall profitability of biopharmaceutical companies.

## **Robust Intellectual Property Rights**

It's difficult to achieve innovation without the protection of knowledge and ideas, and that's particularly the case in an industry whose products require billions to develop in a process that usually takes longer than a decade. This is why IP can constitute up to 80 percent of a life-sciences' company's value.<sup>149</sup> Indeed, IP rights give life-sciences enterprises the confidence needed to undertake the difficult, risky, and expensive process of life-sciences innovation secure in the knowledge they can capture a share of the gains from their innovations, which is

indispensable not only to recouping the upfront R&D costs of a given drug, but which can generate sufficient profits to enable investment in future generations of biomedical innovation and thus perpetuate the enterprise into the future.<sup>150</sup> But not 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.”

Strengths of the U.S. IP regime include clear and comprehensive subject-matter patent-eligibility rules; clear standards for meeting standard patent-eligibility tests of non-obviousness, utility, and capacity for industrial application; the ability to patent both pharmaceutical manufacturing product and process innovations; patent-linkage provisions (which clarify linkages between the patent status of an innovative drug and the granting of marketing approval for a generic medicine referencing the originator product); patent-term extension provisions (to restore the portion of a patent term that may be lost while the patent holder awaits regulatory approval, or for delays in the granting process); trademark and trade-secret protections; and exclusive rights to the underlying clinical trial data that validates the safety and efficacy of novel drugs that continue past patent expiry. The United States also benefits from an effective USPTO to review patent applications and issue patents, as well as a judicial system capable of effectively adjudicating IP disputes.

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**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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Another strength of the U.S. IP system has been its data-exclusivity period for novel biologic drugs. Biologics refer to any pharmaceutical drug product manufactured in, extracted from, or semi-synthesized from biological sources. For the first time in 2020, biologics now account for over 40 percent of the drugs in the global development pipeline.<sup>151</sup>

Unlike traditional pharmaceutical drugs, which involve smaller molecules that operate largely on the basis of chemical reactions and that work by treating the consequences of a disease, biologics work by blocking diseases earlier in their development, in the immune system. And since they can be tailored to individuals taking the medicine, biologics constitute an important step toward realizing the vision of personalized medicine.<sup>152</sup> But as biologics are large, complex molecules that must be manufactured within living tissues, the resulting protein is unique to the cell lines and the specific process used to produce it, and even slight differences in the manufacturing of a biologic can alter its nature.<sup>153</sup> Accordingly, the IP components of a biologic include both the structure of the molecule itself and the process for how to reliably, safely, and consistently manufacture the molecule at scale in living tissues.

While patents constitute one important form of IP protection for biologics, they are not sufficient to support the environment needed to promote large-scale investment in biologic R&D, for two principal reasons. First, because biologics are structurally complex molecules which are closely tied to a specific manufacturing process, many biologic patents are process patents or relatively narrowly constructed product patents. This means that biologics patents are susceptible to being circumvented by small changes to the molecule or to the process of making it.<sup>154</sup> Because

patents fail to provide the same certainty for biologics as they do for traditional pharmaceutical drugs, they do not necessarily assure that biologics will enjoy the same length of time on the market before facing competition from generics. Second, patents do not safeguard the IP involved in developing the extensive clinical trial data and results required to prove the safety and efficacy of a biopharmaceutical product (e.g., the regulatory data).

This creates a situation in which, as Kathleen Kelleher explained in the *Michigan Telecommunications and Technology Law Review*, “The complexity of most biologics may allow a biogeneric manufacturer to design around an innovator’s patents, but still secure regulatory approval through its ‘biosimilarity’ to the pioneer (original) biologic.”<sup>155</sup> In other words, because regulatory approval for biosimilar drugs does not require identity with the pioneer biologic drug it references without an extended period of data exclusivity—which protects the actual investment needed to prove the safety and efficacy of a biopharmaceutical product—a competing biosimilar product could elude the innovator’s patent while still relying on the innovator’s clinical data for regulatory approval, thus creating a “patent protection gap.”<sup>156</sup> (This gap does not exist for small-molecule drugs, which receive five years of data-exclusivity protection, because generic drugs are required to have the *identical* active ingredient.)

As Professor Kristina Lybecker concluded, “Although patent protection and data exclusivity may be considered complementary forms of protection, they serve distinct purposes. Patents are granted for innovations that are novel, non-obvious and useful ... while data protection incentivizes the lengthy development work which is necessary to establish safety and efficacy regulatory approval of a new product.”<sup>157</sup>

Recognizing the need to strike a balance between innovators’ incentives for investment in expensive, risky drug development while at the same time making room for competition by creating a path for biosimilar manufacturers to bring biosimilar products to market, the U.S. Congress extensively debated the appropriate length of regulatory data protection for biologic drugs in the late 2000s. In 2009, recognizing that biologics constitute unique products that merit high levels of IP protection, Congress passed the bipartisan Biologics Price Competition and Innovation Act (BCIPA), which enshrined 12 years of data-exclusivity protection for novel biologic medicines. This protection means that biosimilar manufacturers must independently conduct the comprehensive pre-clinical and clinical trials for their own product, or wait the 12 years required by the Biologics Act before requesting a regulatory shortcut to approval based on the innovator’s prior approval and data.<sup>158</sup>

And the U.S. Congress was not alone in concluding, after extensive deliberation, that biologic drugs merit extended data-protection rules. Congress’s decision relied in part on findings from the National Academies of Science and Engineering report *Rising Above the Gathering Storm*, “It is critical that a balance be struck in finding an appropriate period of exclusivity such that innovation is stimulated and sustained but patients have access to generic-drug-pricing structures,” and recommended that this data exclusivity period should be “at least 10 to 11 years.”<sup>159</sup> U.S. law should continue to provide 12 years of biologics data exclusivity, and U.S. trade negotiators should continue to seek similarly high standards in FTAs.

## **Sufficient Resources to Finance Biopharmaceutical Innovation**

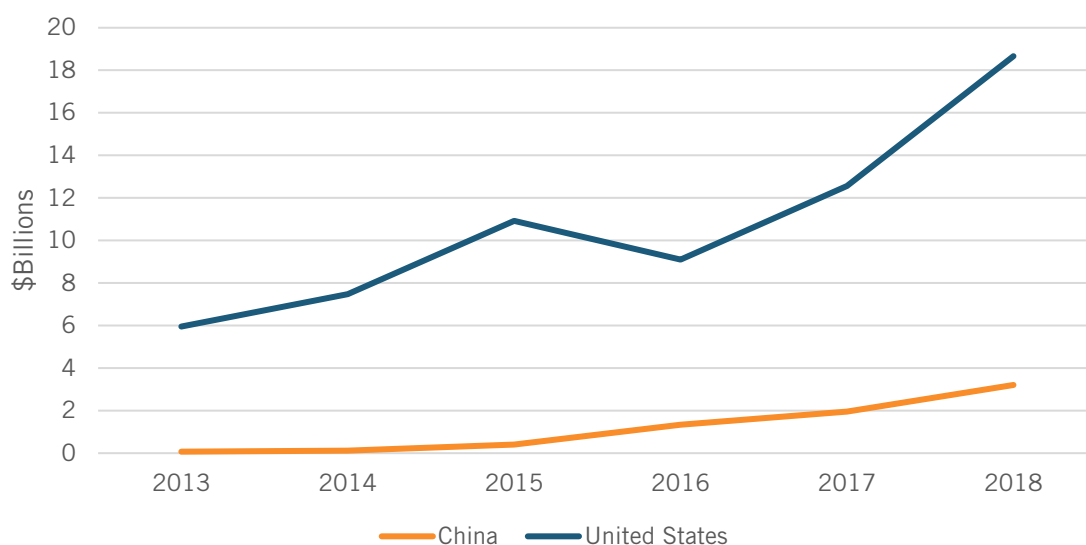
A key strength of America’s life-sciences innovation system has been creating a financial-markets environment capable of both valuing and marshalling the tremendous amount of capital



necessary to finance investment in risky biopharmaceutical innovation. Liquid financial markets provide needed risk capital, especially for start-ups, as well as exit channels in the form of initial public offerings (IPOs) or mergers and acquisitions (M&A). Venture capital (VC) represents a key part of this equation, and is especially important to the creation of high-tech start-ups, providing both the actual funds needed to sustain operations, and experienced business advice to maximize their chances of success.<sup>160</sup> That matters because start-ups account for 66 percent of U.S. biopharmaceutical enterprises, contribute 12 percent of employment, have an average R&D intensity rate of 62 percent, and have a 60 percent 5-year survival rate.<sup>161</sup> Nearly three-quarters of worldwide VC investments in biopharmaceutical companies are made in the United States.<sup>162</sup>

Looking at annual U.S. and Chinese biotechnology and pharmaceutical investment from 2003 to 2018 shows that U.S. VC in this sector more than tripled over the period, to \$18.6 billion, while China's rose from less than \$1 billion to \$3 billion. (See figure 26.)

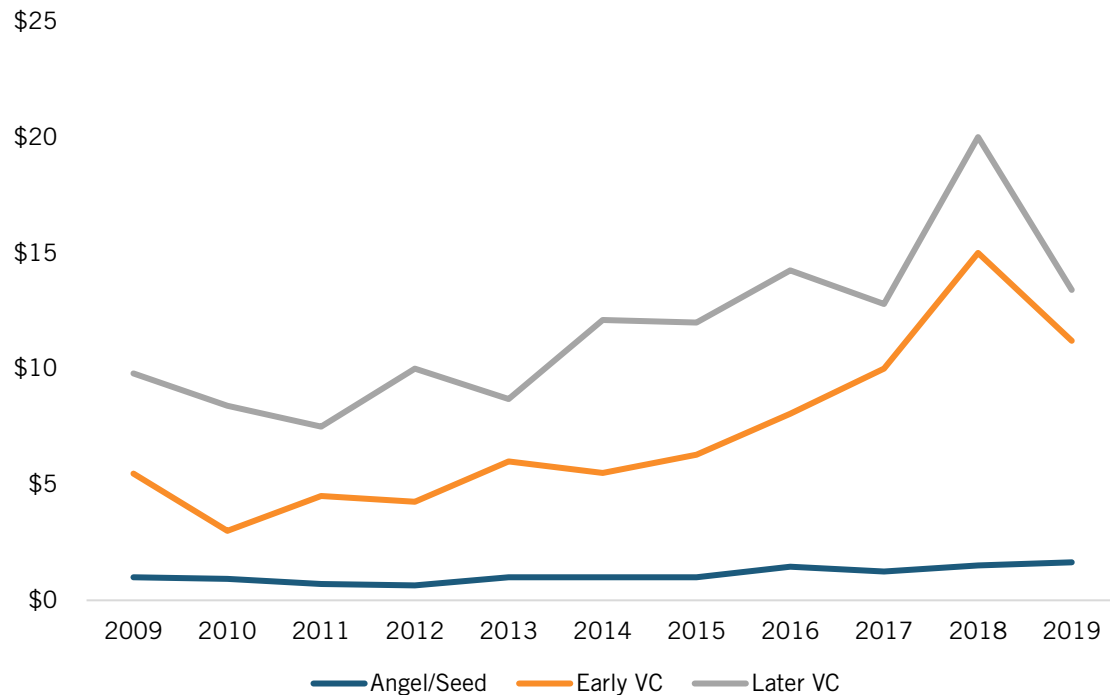
**Figure 26: Annual U.S. and Chinese pharmaceutical and biotechnology venture capital, 2003–2018<sup>163</sup>**



Effective national VC systems should be able to provide capital at different phases of the start-up cycle, from earliest-stage angel or seed capital to later-stage deals. Despite a 2019 dip, the general growth in early-stage VC investment since 2009 has been heartening, as it shows investors have been more willing to back earlier-stage, and thus riskier but perhaps more transformative, investment deals supporting biotech start-ups. (See figure 27.)



**Figure 27: U.S. biotech and pharmaceuticals venture capital by average deal size, 2009–2019 (millions)**<sup>164</sup>



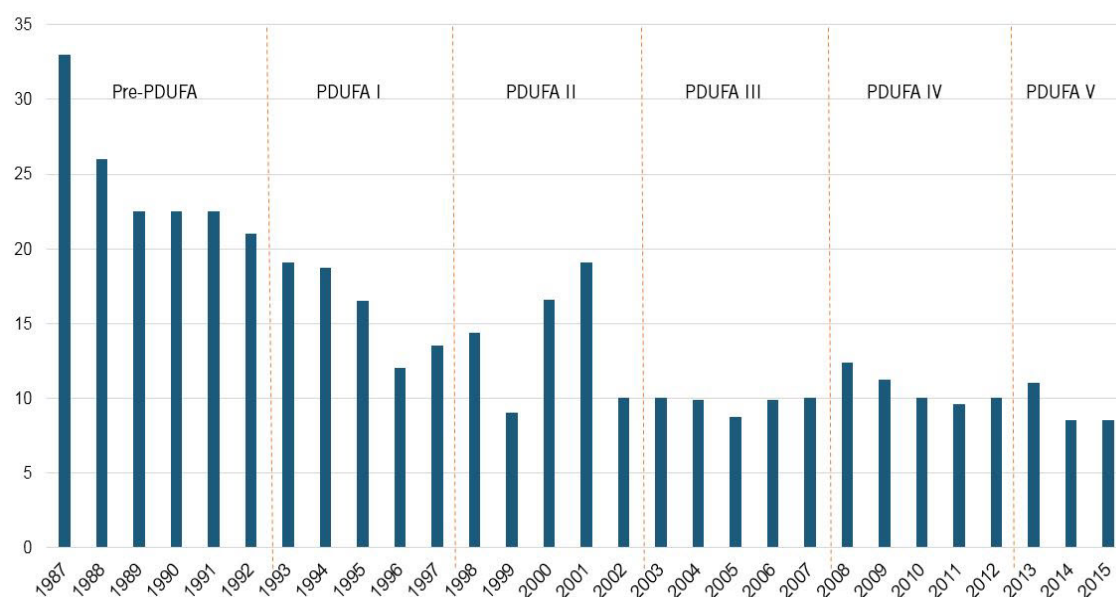
According to Bay Bridge Bio, globally—and referring to biotech start-ups alone—2018 represented the biggest year for biotech VC on record, with \$17 billion invested into biotech start-ups. In 2019, there were 37 significant IPOs of VC-backed biotech start-ups, which raised a total of \$4.2 billion, as well as \$37 billion in acquisitions of biopharma start-ups.<sup>165</sup>

Biopharmaceutical companies are also developing their own corporate VC funds, which can “play an essential role in the sustainability of the biotech ecosystem, advancing the future of pharmaceutical innovation and biotech entrepreneurship.”<sup>166</sup> Between 2008 and 2018, the corporate venture arms of large biopharmaceutical companies contributed to deals totaling over \$39 billion in start-up financing, now accounting for over half of venture investments in the sector, which totaled almost \$74 billion.<sup>167</sup>

### **An Effective Regulatory Drug Approval System**

Lastly, one of the reasons America's life-sciences innovation system lagged behind global leaders in the 1970s and 1980s was a faltering regulatory system that took years to approve drugs and thus in part made the United States an unattractive locale for the introduction of new-to-the world drugs. In fact, in 1987, it took the FDA almost 3 years to make a safety and effectiveness determination for a new drug, but by 2015, the median approval time had fallen to under 10 months. (See figure 28.)

**Figure 28: Median approval times for new medicines, months (CDER NME NDAs/BLAs)<sup>168</sup>**



The difference was bipartisan congressional legislation, originally introduced in 1992, creating PDUFA, which authorizes the FDA to collect user fees associated with applications from the biopharmaceutical industry for regulatory approval of new human drug submissions.<sup>169</sup> The user fees generated by PDUFA are intended to supplement, not replace, congressional appropriations, although fees generated by PDUFA now account for more than 70 percent of the FDA’s funding for reviewing new drug applications. Over the quarter-century since its founding, and through six congressional reauthorizations, PDUFA has provided the FDA with a stable, predictable funding stream that has contributed to significantly accelerated review times and created new pathways for swifter review of high-impact drugs, particularly through a “breakthrough therapy” designation intended to expedite the development and review of drugs for serious or life-threatening conditions.<sup>170</sup>

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**In 1987, it took the FDA almost 3 years to make a safety and effectiveness determination for a new drug, but by 2015, the median approval time had fallen to under 10 months.**

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Though certainly not the only factor, PDUFA has been an important part of the reason why innovative new drugs tend to reach patients faster in the United States than in Europe or elsewhere. For instance, Roberts, Allen, and Sigal wrote in one study that “the median time for approval for new cancer medicines in the United States was just six months—and that these new anticancer medicines are typically available in the United States before they are in Europe.”<sup>171</sup> PDUFA has played an important role in encouraging more companies to launch new drugs first in the United States, meaning U.S. patients have the earliest access to them, while being at least equally as good as other regulatory agencies (such as the European Medicines Agency) at not approving drugs that turn out to be dangerous.<sup>172</sup>

PDUFA VI, passed by Congress in 2017 and which covers FY 2018–2022, made significant enhancements to PDUFA along several dimensions, including prioritizing the development of

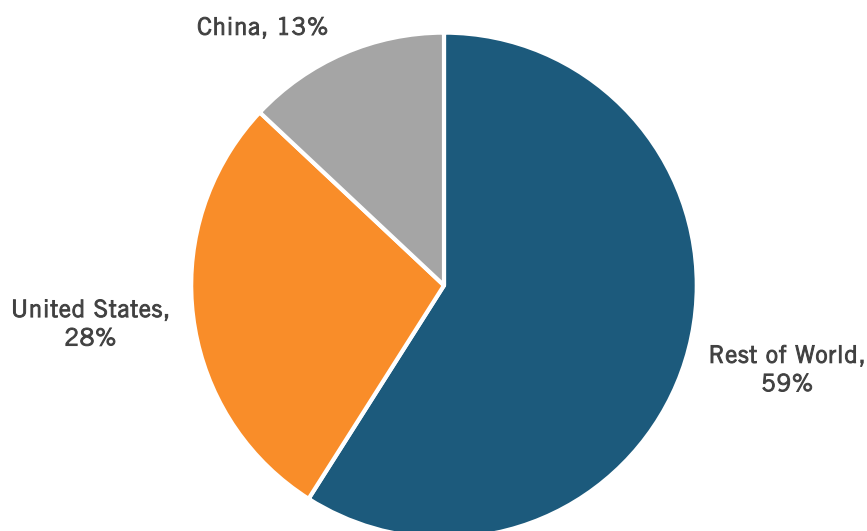
breakthrough medicines for patients with life-threatening diseases, supporting innovative clinical-trial approaches, enhancing the drug development and approval process for rare diseases, making greater use of real-world evidence in regulatory decision-making, enhancing post-market safety monitoring of approved drugs, and streamlining workflow and workforce process planning at the FDA.<sup>173</sup> In conclusion, PDUFA constitutes a key backbone of the U.S. life-sciences innovation system, and Congress should continue to look favorably upon it in future reauthorizations.

## RESHORING OR GLOBAL SUPPLY CHAINS? OR BOTH?

While the pandemic has raised concerns about U.S. dependency on foreign nations for key biopharmaceutical, medical device, and medical supplies goods, in general, overall U.S. dependence on foreign suppliers of drugs may be overstated.<sup>174</sup> For instance, 75 percent of U.S. spending on drugs goes to medicines that have been produced domestically in the United States, while an estimated 70 percent of the medicines actually consumed in the United States are manufactured domestically.<sup>175</sup>

Moreover, the U.S. supply chain for medicines that are imported is actually quite diverse, with more than 90 countries supplying the United States with pharmaceutical products. In 2019, 73 percent of U.S. imports of pharmaceutical products came from Europe, while 61 percent of imported APIs came from European sources. In fact, last year, the United States actually sourced 40 percent more of its imported APIs from Ireland than it did from China. As CDER Director Janet Woodcock stated in 2019 congressional testimony, “CDER’s analysis shows that overall, China has only a modest percentage of the facilities able to produce APIs for the U.S. market.”<sup>176</sup> As she noted, for all regulated drugs, China has 230 (13 percent) of the API manufacturing facilities, while the United States has 510 (28 percent), and the rest of the world has 1,048 (59 percent). (See figure 29.)

**Figure 29: Percentage of API manufacturing facilities for all regulated drugs by region, August 2019<sup>177</sup>**



The American Action Forum found that China supplies only 18 percent of total U.S. API imports, 9 percent of total antibiotic imports, and less than 1 percent of total vaccine imports.<sup>178</sup> The report asserts that U.S. production is often understated, in part because of data limitations. For example, 70 percent of total antibiotic spending and 50 percent of total vaccine spending is on U.S.-made products.

In addition, global value chains facilitate the development and production of a wide range of advanced-technology products, from airplanes and semiconductors to medical devices and pharmaceuticals. Modern supply chains are characterized by extremely high degrees of specialization that enable the production of complex technology products at the lowest cost/highest capability possible.<sup>179</sup> For instance, the production of the ventilators so critical to saving the lives of patients in the coronavirus crisis entails incorporating as many as 700 parts and components sourced from vendors from throughout the world.<sup>180</sup>

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**Calls for massive reshoring ignore the fact that it makes sense to rely on global supply chains for at least some manufacturing production.**

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To be fair, China is a different matter. China is virtually alone in its potential willingness to use export bans to achieve political and economic goals, as it has done with its prior ban on the export of rare-earth minerals. At the same time, China has made it clear that it seeks global dominance in drug production.<sup>181</sup> As such, policies to encourage supply chains to shift out of China make sense.

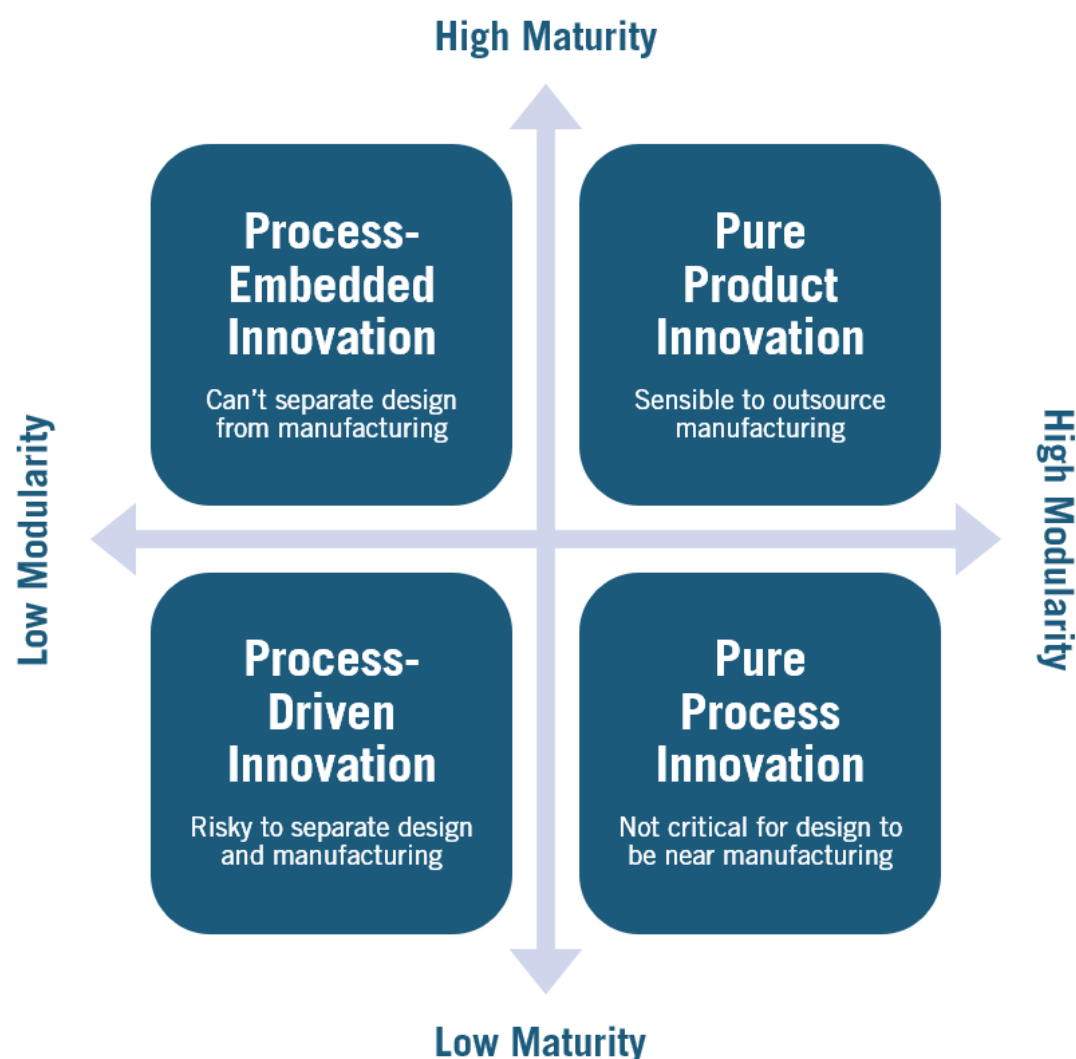
At the same time, calls for massive reshoring ignore the fact that it makes sense to rely on global supply chains for at least some manufacturing production. One useful framework for thinking about this comes from Harvard Business School professors Gary Pisano and Willy Shih. They have argued that the degree to which it makes sense to offshore production or keep it at home depends on two factors: process maturity (the extent to which the technologies used to produce a product are mature or continuing to evolve) and modularity (the degree to which information about product design can be separated from the manufacturing industry). (See figure 30.)

Their argument is that in industries with high modularity and mature production processes, offshoring in order to lower costs makes good business sense and does not come at the cost of product or process innovation. They put the production of APIs in this category; the production process is relatively mature and product innovation (the development of new drugs) is not dependent on close linkages to the production process. This is why a significant share of API production has moved offshore. In contrast, they've argued that biotechnology production (the production of large-molecule, living compounds) is not a mature production process and there are closer links between drug development and drug production. This is why a much larger share of biotechnology production is still in the United States.

There are at least five main policy implications from this. The first is that to the extent that policy can spur more drug innovation, especially in large-molecule, biotech drugs, the more likely it is that production will locate in the United States. The converse is also true: The more there is a push to replace novel drugs with generics, the more likely that supply will be filled through offshore production. As Shih and Pisano wrote, in sectors developing breakthrough products at the

frontiers of science, the major process innovations are evolving rapidly and are critical to product innovation.

**Figure 30: Pisano and Shih's “Modularity-Maturity Matrix” for offshoring/outsourcing decisions<sup>182</sup>**



As Shih and Pisano continued, “Biotechnology offers a good example. Drugs derived from genetic engineering techniques consist of large protein molecules that are too complex to be chemically synthesized—the approach used to make drugs for over a century. Without major advances in process technology (such as mammalian-cell-culture processes), blockbuster drugs like Amgen’s erythropoietin, for treating anemia, or Genentech’s Herceptin, a therapy for breast cancer, would never have made it out of the laboratory.”<sup>183</sup>

Moreover, in this kind of production, low wages are less of an advantage. One study modeled the cost of producing CAR-T biotech therapies in four locations, including in two low-cost nations. It found that even though labor costs were higher in the United States, the differences in total costs of production were relatively small, in part because of the high cost of inputs and the role that automation will play.<sup>184</sup>

There are very good reasons for a greater number of active government policies. As Shih and Pisano wrote: “Managers, investors, and analysts haven’t always recognized this danger. Viewing manufacturing as a distraction and a drain on capital, they often push companies in this quadrant to outsource production or move it to lower-cost locations far away from R&D. The results can be disastrous because, to put it simply, when you lose your manufacturing competence, you lose the ability to create new commercially viable products.”<sup>185</sup> Policies that encourage, rather than mandate, more production at home, can not only lead to more domestic production and jobs, but also support more drug innovation.

Second, spurring more process innovation is important because it can move a part of the industry from the upper-right quadrant where reshoring makes more sense to the lower-left quadrant where it makes less sense. That is why, as discussed ahead, the Information Technology and Innovation Foundation (ITIF) recommends significant public investments, in partnership with industry, in biopharmaceutical process technology innovation, including innovations in continuous process production systems, and also greater automation. As Shih and Pisano wrote, “When a company operates in a sector where the process technology is mature, it’s tempting to dismiss the possibility of process innovation and try to reduce costs by outsourcing or offshoring production. But game-changing process technologies sometimes can emerge.”<sup>186</sup> As another study notes, continuous process innovation offers a “[h]igh potential for enhanced domestic manufacturing, which includes supply chain and security benefits. This is because unlike batch processes, continuous processes do not depend on low-cost labor, but instead on advanced technology.”<sup>187</sup> And related to the current focus on drug supply chains, the study’s authors noted that continuous production technologies would increase the “[a]bility to respond much more agilely to drug shortages and related challenges including decreasing the risk of having sole suppliers for essential medicines.”<sup>188</sup>

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**Washington needs to make a commitment that it will win in this industry. If it decides to do so—and there are plenty of reasons, including national security, to want to win—policymakers should adopt an industry competitiveness agenda.**

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Third, to the extent offshoring decisions are made on the basis of foreign unfair trade practices, the U.S. government should work more actively against them. In the 2000s, some of the expansion of Chinese API production was facilitated by Chinese government currency manipulation that made Chinese exports cheaper. To the extent that foreign API production, especially in low-wage nations such as China and India benefit from regulatory asymmetries, especially limited FDA inspections and imports of counterfeit drugs, U.S. government policy should remedy this.

Fourth, efforts to force production that is in the upper-right quadrant to locate in the United States will have negative impacts, raising the price of drugs—something policymakers actively want to work against—while at the same time reducing U.S. competitiveness globally. This is why calls for Buy American provisions for drugs represent the wrong solution. A better solution is to use incentives to spur more reshoring. Not all production will be able to move back given the significant cost advantages of producing in low-wage nations, but some will be able to with the right incentives, as described ahead, because total production cost differentials are not all that

high. It is in this context that the repeal of Section 936 of the tax code that enabled significant production in Puerto Rico was a mistake.

## POLICY RECOMMENDATIONS

While the United States may lead in biopharma innovation, that lead is being challenged by a host of nations using legitimate and illegitimate policies and tactics. (For a comprehensive list, see appendices A and B, respectively.) Moreover, U.S. production capabilities have weakened. If the United States wants to avoid having its biopharma industry follow the same tragic path of once-strong industries such as telecommunications equipment, machine tools, solar panels, and others, it must want to actively compete and to win. In other words, Washington needs to make a commitment that it will win in this industry. If it decides to do so—and there are plenty of reasons, including national security, to want to win—policymakers should adopt an industry competitiveness agenda. This should start by maintaining U.S. policy strengths.

### Maintain U.S. Policy Strengths

As noted, the United States has done many things right when it comes to policies to support a robust biopharma ecosystem. First and foremost, the United States needs to preserve and protect the policies that are already effectively working.

### Eschew Drug Price Controls

Let's start with the most controversial issue: drug pricing. The harsh reality is that if the United States wants to maintain, much less grow, its biopharma industry, strict drug price controls will make that extremely difficult. Innovators want to be and are able to innovate in the United States because they know that if they are successful with a new drug—which, more than often, is not the case—they stand a reasonable chance of making a good return on investment. As industrial organization economist F.M. Scherer wrote, “Had the returns to pharmaceutical R&D investment not been attractive, it seems implausible that drug-makers would have expanded their R&D so much more rapidly than their industrial peers.”<sup>189</sup>

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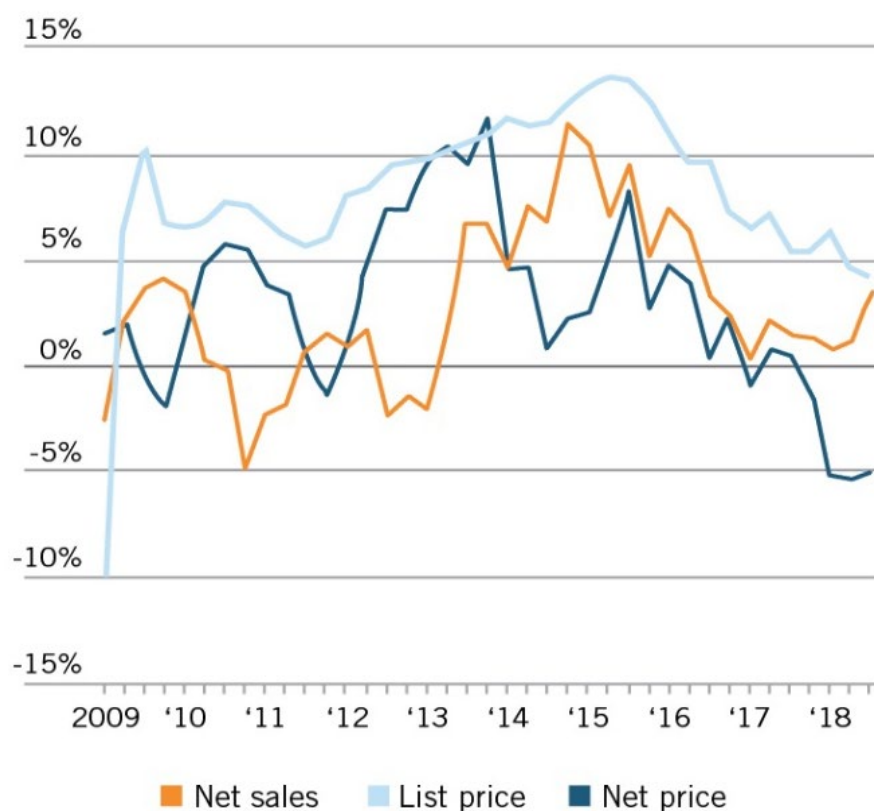
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The issue of prescription drugs is an important one, especially regarding affordability for many individuals. But it is less of an issue in the context of the overall increase in health care spending. In 2018, prescription drugs accounted for just 9 percent of total U.S. health spending, up only modestly from the 7 percent share of total spending they accounted for in 1970.<sup>190</sup> Moreover, while the list prices of prescription medicines are often referenced, the net prices paid are often considerably lower. *The Wall Street Journal*, citing data from the SSR Health Report, noted, “[A]verage U.S. list prices for prescription medicines rose in the past decade, but net prices—after rebates and discounts—rose less sharply and have recently declined.”<sup>191</sup> (See figure 31.) In fact, one study found that more than one-third of drug list prices were rebated back to pharmacy benefit managers and other entities in the supply chain.<sup>192</sup> As that report describes, “Pharmaceutical spending estimates that omit rebates and discounts do not fully reflect the underlying competitive dynamics of the pharmaceutical sector and provide a misleading impression of drug spending.”<sup>193</sup>



Moreover, U.S. biopharmaceutical manufacturers fundamentally do not realize outsized returns. In fact, over the past decade, as Deloitte’s report “2020 Global Life-sciences Outlook” finds, drug intermediaries and retailers have consistently earned higher returns on investment than the biopharmaceutical and medical device manufacturers who are actually innovating new-to-the-world, life-saving or life-improving drugs and medical devices.<sup>194</sup> (See figure 32.) Among enterprises in U.S. health care industries, life-sciences companies actually experienced the biggest drop in returns on capital (ROC), from 17 percent in 2011 to 11 percent in 2017. As the Deloitte report concludes, “[L]ife-sciences companies demonstrated lower ROC than other organizations in the health care ecosystem, such as drug intermediaries and retailers, over the seven-year period.”

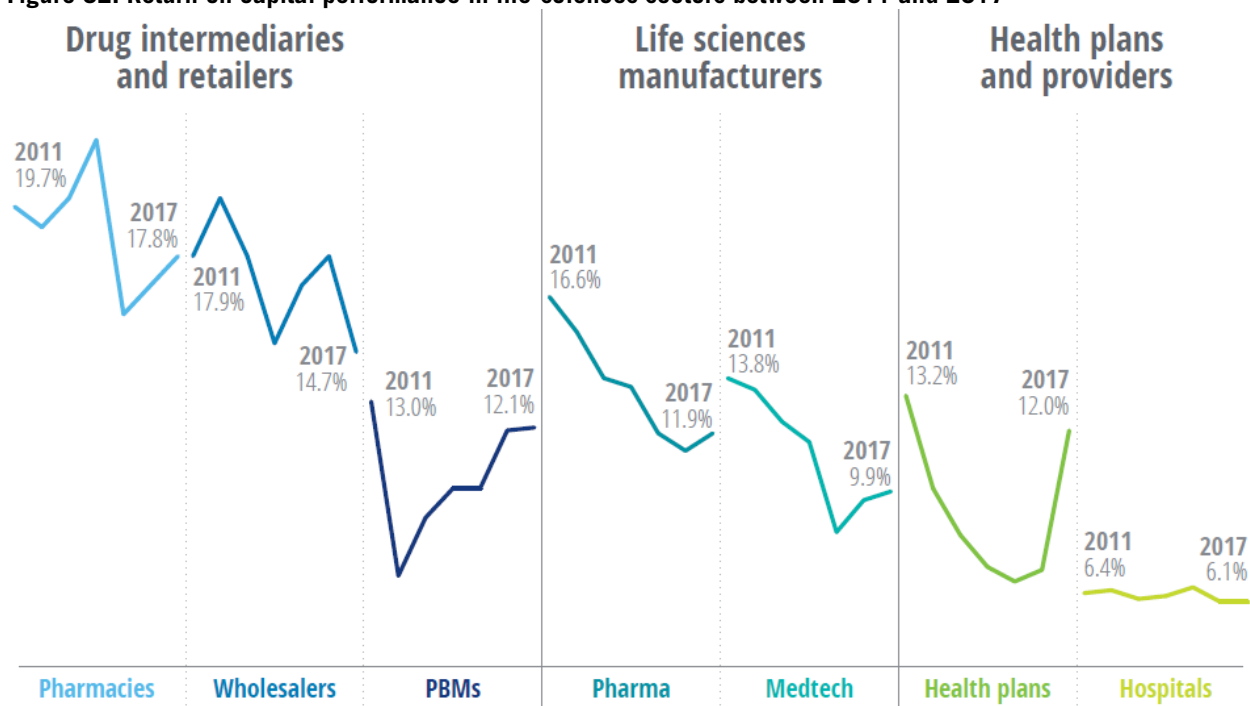
**Figure 31: Change from a year earlier in U.S. prescription brand prices<sup>195</sup>**



Moreover, the United States has effectively implemented a life-science innovation that promotes breakthrough innovation and then facilitates generic competition to help manage drug prices. In fact, in 2018, generic drugs accounted for approximately 90 percent of U.S. prescriptions (85.6 percent unbranded generics and 4.3 percent branded generics).<sup>196</sup> As Jack Scannell, a senior fellow at Oxford University’s Center for the Advancement of Sustainable Medical Innovation (CASMI), has explained, “I would guess that one can buy today, at rock bottom generic prices, a set of small-molecule drugs that has greater medical utility than the entire set available to anyone, anywhere, at any price in 1995.”<sup>197</sup> He continued, “Nearly all the generic medicine chest was created by firms who invested in R&D to win future profits that they tried pretty hard to maximize; short-term financial gain building a long-term common good.”<sup>198</sup>



**Figure 32: Return on capital performance in life-sciences sectors between 2011 and 2017<sup>199</sup>**



On September 14, 2017, the FDA approved Mvasi, the first biosimilar for Roche’s Avastin, a breakthrough anti-cancer drug for lung, cervical, and colorectal cancers.<sup>200</sup> In other words, a drug capable of treating various forms of cancer that scarcely existed 20 years ago is now available as a generic drug. It’s that dynamic that enables us to envision a future wherein drugs are available at generic prices in 2040 for a set of innovative drugs that have greater medical utility than the entire set available to anyone, anywhere, at any price in 2020. But this dynamic will only persist if policymakers refrain from introducing drug price controls that would preclude life-sciences innovators from earning sufficient revenues from one generation of biomedical innovation to invest in the next.

As noted, drug price controls will come at the cost of drug innovation. In this sense, drug prices represent a trade-off between the interests of present and future generations: We could price all drugs that now exist at their marginal cost today, but that would leave no revenues to invest in future generations of biomedical innovation. **Accordingly, the Trump and future administrations should not introduce drug price control schemes, such as HHS’s proposed International Pricing Index Model for Medicare Part B Drugs.**<sup>201</sup>

### Preserve the Bayh-Dole Act

As noted, the Bayh-Dole Act has played a catalytic role in stimulating U.S. life-sciences innovation. However, some policymakers and civil society advocates have proposed leveraging Bayh-Dole march-in rights to allow the government to exert influence over drug prices when a drug can trace any part of its provenance to federal R&D funding, arguing that “reasonable terms” language associated with march-in rights permits this.<sup>202</sup> This despite the fact that the law’s architects, Birch Bayh and Bob Dole, have publicly stated that their intent with march-in rights was to ensure that products were licensed on reasonable terms rather than being used as a price control (in other words, that march-in rights pertain to reasonable licensing terms).<sup>203</sup>

Starting in 2017, NIST undertook a review of federal policies facilitating technology transfer and commercialization, with the review culminating in April 2019 with the green paper “Return on Investment Initiative for Unleashing American Innovation.”<sup>204</sup> With regard to the issue of march-in rights in the Bayh-Dole Act, the green paper writes, “The use of march-in is typically regarded as a last resort, and has never been exercised since the passage of the Bayh-Dole Act in 1980.”<sup>205</sup> It goes on to note, “NIH determined that that use of march-in to control drug prices was not within the scope and intent of the authority.”<sup>206</sup> It concluded, “Overall, stakeholders agreed that the march-in authority should not be broadened, and that doing so would create uncertainties in the U.S. innovation system.”<sup>207</sup> **NIST is expected to clarify the meaning of “reasonable terms” as it relates to Bayh-Dole Act march-in rights later this year, and it should affirm the understanding that the price of resulting products is not an adequate basis for the exercise of Bayh-Dole march-in rights.**

### Maintain PDUFA

The effectiveness of the original PDUFA and its predecessors has played a transformative role in making America an attractive environment for life-sciences innovation. The current PDUFA, PDUFA VI, will run through September 2022 (the Act is renewed in five-year increments).

**Congress should look positively upon PDUFA, and when the time for PDUFA VII arrives, look to embrace lessons from the coronavirus crisis in terms of seeking innovative models of clinical trial design, embrace real-world evidence in clinical trials, and streamline and enhance the operational capacity of the FDA.**

### Fully Fund the Patent Office

USPTO is funded entirely by user fees and does not receive tax dollars; however, the office does require an appropriation from Congress to spend the money it collects.<sup>208</sup> Ensuring continued smooth operation of USPTO is critical to the functioning of the U.S. patent system. As it has acknowledged, the U.S. Treasury currently holds some fees collected but that have not been apportioned to USPTO. (That does represent progress, as previously appropriators in Congress had not acknowledged the funds were “real.”) **The U.S. Treasury should apportion these funds to USPTO with alacrity.** This is especially important because the funds represent money collected by users of USPTO and, moreover, when the practice of fee diversion ended, these funds should have been already appropriated. Doing this presently would be very beneficial to USPTO, which has experienced a significant decline in revenue and fees collected due to the coronavirus crisis.

### Expand and Adopt New Policies to Spur Greater Levels of Domestic Innovation

While America should maintain the policies that have worked, absent new and expanded initiatives, the risk of the United States losing its lead will grow. As such, there are several steps Congress should take.

### Boost NIH Funding

As noted, public and private investment in life-sciences research is strongly complementary. The federal government is underinvesting in life-sciences R&D compared with historical norms, in part because investment has not been keeping up with inflation. **Congress should at least restore NIH funding to 2003 levels as a share of GDP, which would entail boosting NIH funding by \$11.6 billion per year.**<sup>209</sup> **Congress could close the federal R&D underinvestment gap in the life-sciences and other sectors by passing the bipartisan Endless Frontiers Act,** sponsored by senators Schumer (D-NY) and Young (R-IN) in the Senate and representatives Gallagher (R-WI) and Khanna (D-CA) in the

House, which would invest \$100 billion over 5 years across a number of advanced-technology sectors—including biotechnology, genomics, and synthetic biology—as well as designate at least 10 regional technology hubs to ensure continued American leadership in the advanced technologies that will drive future economic prosperity.<sup>210</sup>

### Support R&D Megafunds

In 1960, private-sector R&D was split about one-third to basic research and two-thirds to development; today, only about one-fifth of enterprise R&D goes to basic research. One reason companies are moving away from basic and applied research is the risk involved in financing. In drug development, as noted, it often takes over a decade and hundreds of millions, if not billions, of dollars to produce a profitable product. Individual companies and even venture capitalists often lack the appetite for such long-term, high-risk investments.<sup>211</sup>

This risk could be mitigated through large portfolios that aggregate and manage risk. Mutual funds, pension funds, and 401(k) retirement accounts work this way. MIT economist Andrew Lo has proposed extending this idea by establishing “megafunds” that utilize financial engineering techniques to fund R&D in long-term, high-risk, high-payoff areas such as drug discovery for cancer or orphan diseases.<sup>212</sup> However, to date, no such megafunds have been created by the market. The government incentives required for the creation of these funds could include one or more approaches from four broad categories: research and investment data streams; clear rules for private-foundation program-related megafund investments; federal credit support; and tax incentives for funds investing in drugs (e.g., through the establishment of schedules and values of basis-point step-ups and penalties).

**To promote the creation of R&D megafunds, the Department of Commerce should establish an office to develop and implement the needed incentives and oversight for the creation of megafunds.** The office would be tasked with establishing the rules for the funds and coordinating with federal agencies and the private sector to identify the technical areas of national interest wherein private-sector engagement is needed and incentives required.

### Increase and Establish Incentives for R&D and Innovation

The billions of dollars needed to produce new-to-the world drugs today merit compelling tax and investment incentives to help defray the significant up-front R&D costs. Accordingly, Congress should leverage the tax code to encourage greater levels of medicines and medical device manufacturing in the United States. First, **Congress should at minimum double the of rate of the Alternative Simplified Credit (R&D) from 14 percent to 28 percent.**<sup>213</sup> Congress could stimulate greater levels of industry R&D investment to take place at U.S. universities by **amending the existing collaborative R&D tax credit to allow companies to take a flat 20 percent tax credit when they invest in university R&D activity.**<sup>214</sup> (Currently, America’s collaborative R&D tax credit applies only to energy investments.) This is especially important because the life-sciences sector is the largest scientific field for U.S. university R&D spending, accounting for nearly three-quarters of R&D investment by universities, or \$68.2 billion, in fiscal 2017, with \$4.8 billion contributed by industry.<sup>215</sup> **Congress could stimulate further investment in rare-disease R&D and innovation by restoring the orphan drug tax credit to 50 percent.**

While the tax code’s primary mechanism facilitating innovation is the R&D tax credit, the credit is less useful for pre-revenue companies because it requires tax liability, which requires income.<sup>216</sup> In other words, the tax credit is designed more for established innovators, not so

much for research-intensive, pre-revenue companies that are trying to develop new technologies such as medical devices or biopharmaceutical drugs. These are extremely R&D-intensive companies, which tend to invest 75 percent or more of their expenditures in R&D.

Firms in this position often find it difficult to raise the capital needed to get them through the long development phase until they are near enough to profitability to conduct an initial public offering or be attractive to a prospective buyer. The PATH (Protecting Americans From Tax Hikes) Act of 2015 made the R&D tax credit permanent, and allowed small businesses to take the credit against their payroll taxes. But two additional tax reform proposals could further address these challenges.

The first proposal would amend Section 469 of the tax code to permit passive investors to take advantage of the net operating losses and research tax credits of companies in which they invest.<sup>217</sup> (The Tax Reform Act of 1986 severely limited this ability because it was seen as a way for high-income individuals to reduce their taxes by investing in operations that were never meant to be profitable.) Under this reform, investors could immediately use their share of net operating losses, as well as any credits for R&D. The percentage of losses or credits that could be passed through would be limited to the portion of investment that was specifically targeted for qualified research activities as determined for purposes of the R&D tax credit. In order to qualify, a company would have to devote at least half of its expenses to R&D. The company would also have to have fewer than 250 employees and less than \$150 million in assets. A recent study by Ernst & Young estimates that this change would increase investment in such companies by \$9.2 billion, allowing them to create 47,000 jobs.<sup>218</sup>

The second change would make it easier for small companies to carry net operating losses forward even as they continue to attract new investors. Small, research-intensive companies often go through several rounds of financing as they rack up expenses while getting nearer to their goal of profitability. Unfortunately, Section 382 of the tax code prevents companies from carrying net operating losses forward if they undergo an ownership change. This rule eliminates an attraction to investors. It also means that those companies will start paying taxes on their revenue long before their total revenues exceed total expenses. Under the proposed change, Section 382 would not apply to net operating losses generated by qualifying R&D activities conducted by small businesses. The Ernst & Young analysis estimates that this change would increase direct investment in these companies by \$4.9 billion and boost their employment by 25,000 jobs.<sup>219</sup>

### Support Data-Driven Drug Development

The advent of big data and artificial intelligence (AI) is likely to facilitate the drug-discovery process. It represents one of the many approaches being taken to try to improve R&D productivity in the biopharmaceutical industry.<sup>220</sup> From screening chemical compounds to optimizing clinical trials to improving post-market surveillance of drugs, the increased use of data and better analytical tools such as AI hold the potential to transform drug development, leading to new treatments, improved patient outcomes, and lower costs.<sup>221</sup> As of November 2019, at least 43 biopharma companies were using AI for drug discovery, including by partnering with AI start-ups.<sup>222</sup> But achieving the full promise of data-driven drug development will require Congress to take several steps to address a number of obstacles.

First, **Congress should direct HHS to implement a unique patient identifier, as originally intended by HIPAA.** Though electronic health record usage is commonplace, health care providers do not have an accurate and efficient method of matching patients' records across different systems.

Second, **policymakers should enforce the publication of data from clinical trial results by directing agencies such as the FDA and NIH to be more aggressive about penalizing noncompliance.** The FDA's finalized rule for penalizing noncompliance went into effect in January 2018, but according to a January 2020 report by researchers at the University of Oxford, compliance with the rule is poor, and not improving.<sup>223</sup>

Third, **Congress should direct HHS to create a model for data trusts that facilitates data sharing among biopharmaceutical stakeholders involved with data-driven drug development.** This model can be adapted from data trusts being developed in other countries, such as the United Kingdom.

Fourth, **policymakers should increase the availability of new kinds of data from nontraditional sources, such as biometric, lifestyle, and environmental data.** This could be supported by fully funding NIH to accelerate the development of the All of Us Research Program's million-person research cohort.

Fifth, **policymakers should direct the FDA to develop best practices for data collection in health care to ensure equitable outcomes, such as strategies to increase coverage of underrepresented populations.**

Finally, **policymakers should facilitate the modernization of outdated regulatory processes.** The process of drug discovery has been internationalized, with discovery, testing, and commercialization taking a multi-country approach. Congress should ensure the FDA has the resources necessary to increase foreign clinical trial inspections, harmonize regulatory standards across national lines to meet the FDA's satisfaction, and adopt risk-assessment analytics tools to prioritize inspections for high-risk sites.

Overcoming these obstacles should be a priority for policymakers because enabling data-driven drug development would not only accelerate access to more effective and affordable treatments for Americans, but help maintain the competitiveness of the U.S. biopharmaceutical industry.

### Expand R&D Talent

Biopharmaceutical innovation rests on highly skilled scientists and engineers. Policy needs to both support the expansion of domestic talent as well as enable the right kind of high-skill immigration. Increasing linkages with industry for doctoral STEM students can improve the quality of research and education. To increase these linkages, **Congress should appropriate \$20 million per year for the establishment of an NSF-Industry Ph.D. Fellows Program to support an additional 1,000 Ph.D. students in STEM fields.**<sup>224</sup> The new NSF-industry program would work by enabling industry to contribute \$20,250 toward each fellowship, in whatever field(s) each company chooses. NSF would match industry funds dollar for dollar.<sup>225</sup>

While home-grown talent is indispensable to U.S. life-sciences leadership, so too is the ability to attract international talent. Accordingly, **Congress should make it easier for foreign graduates with a STEM degree to receive a green card.**<sup>226</sup> Likewise, the L-1 visa stimulates U.S. innovation as "a non-immigrant visa for intra-company transfers for candidates who are already working for the company that intends to open or expand operations in the U.S. It could also be the U.S. parent

company that wants one of its employees working in its subsidiary to work in the U.S.”<sup>227</sup> **The federal government should not restrict L-1 visas.**

### Collaboration to Increase Efficiency in Drug Development

The high and increasing cost of drug R&D does affect the cost of drugs. Accordingly, one of the most important ways to better manage drug prices would be to enhance R&D efficiency in drug research, in other words, to find collaborative ways to work together to make the cost of innovating new drugs less expensive.<sup>228</sup> Most expensive for companies are candidate drugs that reach Phase III clinical trials and then fail; better success at weeding out those types of drugs earlier in the R&D process would make the entire drug discovery process more efficient and less expensive. One important step in this regard has actually been the PDUFA. By putting in place mechanisms that allow drug developers to have frank conversations with regulators about the technical and scientific expectations for a drug to clear certain clinical trial hurdles, it has streamlined the drug-review process to some degree and helped drug developers make better decisions about the likelihood of candidate drugs passing the clinical-trial gauntlet. Congress’s 2017 reauthorization of PDUFA (PDUFA VI) also placed greater focus on supporting rare diseases and breakthrough therapies, including continued application-fee waivers and advanced reviews for medicines that can treat rare diseases, as well as prioritizing the development of breakthrough medicines for patients with life-threatening diseases. In addition, **federal support for joint industry-university research efforts on biopharma R&D efficiency and effectiveness should be expanded.** For example, see MIT’s NEW Drug Development ParadIGmS (NEWDIGS) program, which is “a unique collaborative ‘think and do’ tank focused on enhancing the capacity of the global biomedical innovation system to reliably and sustainably deliver new, better, affordable therapeutics to the right patients faster.”<sup>229</sup>

### Support Policies to Spur Increased Domestic Production

It’s clear that America needs to expand domestic production of drugs, not only for competitiveness reasons, but also national security. Indeed, the coronavirus crisis has exposed potential gaps in America’s capacity to domestically produce certain drugs or their key compounds, active pharmaceutical ingredients. But the response should not be to introduce Buy American policies, which would increase the price of U.S. drugs and exports, as well as encourage other nations to adopt similar policies. Rather, policies to spur R&D in “process innovation” (how a good is produced) as well as new domestic production incentives are needed.

### Support R&D for Process Innovation

Increased biopharmaceutical process innovation can make it more attractive and cost effective to manufacture drugs and APIs in the United States. Indeed, higher U.S. labor costs can be offset by using and investing in more and better machinery, which in turn would lead to a virtuous cycle of production: higher profits, which can lead to higher wages, leading to better machinery and organization of work, and higher skills. As Drew Endy, a member of the bioengineering faculty at Stanford University, explained, “America could disrupt the currently dominant batch manufacturing processes used to make APIs with a less capital-intensive continuous-manufacturing process based on flow chemistry.”<sup>230</sup>

The opportunity here is significant. One study contends that pharmaceutical manufacturing is expensive, inefficient, and non-innovative, with firms using outdated production techniques and



old plants.<sup>231</sup> The study estimates modern biomanufacturing techniques could eliminate as much as \$50 billion in annual production costs.

Another reason why greater investment into R&D process innovation is needed is because productivity growth in the U.S. pharmaceuticals and medicines industry has significantly lagged over the past several decades. According to the Bureau of Labor Statistics, since 1987 (to 2019) labor productivity in the pharmaceuticals and medicines sector actually fell by 0.8 percent a year, the worst performance by any U.S. manufacturing industry.<sup>232</sup>

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**One of the most important ways to better manage drug prices would be to enhance R&D efficiency in drug research.**

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Nevertheless, some progress is being made. Merck, for example, plans to use portable manufacturing units, robotics to improve compliance, data analytics and information technology (IT) integration, and continuous manufacturing in its future operations.<sup>233</sup> Further along, CONTINUUS Pharmaceuticals is working on an integrated continuous manufacturing solution that takes raw material, creates the desired API, purifies the API, and produces the final dosage form in a single system that can operate 24/7. A prototype reduced costs by 30–50 percent, solvent use by more than 60 percent, energy costs by 50–60 percent, facility footprint by about 90 percent, and lead time from months to less than 48 hours.<sup>234</sup>

The federal government has invested in several initiatives to enhance U.S. biomanufacturing competitiveness. One is the FDA’s Emerging Technology Program, launched in late 2014, which advances the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other relevant stakeholders, starting from early technology development.<sup>235</sup> Another is NIIMBL, one of America’s 14 Manufacturing USA Institutes of Manufacturing Innovation, which promotes the development of breakthrough biomanufacturing processes and supports the development of standards that enable more-efficient and rapid manufacturing capabilities.<sup>236</sup> NIIMBL seeks to create test beds to pilot and validate innovative new pharmaceutical manufacturing approaches, in effect “de-risking” them before their adoption by industry. However, funding levels come nowhere near matching the need, with NIIMBL initially operating from \$70 million in federal funding and raising \$125 million in private investment.<sup>237</sup> NIST also recently awarded \$8.9 million for high-impact manufacturing projects related to COVID-19 treatments.<sup>238</sup>

**Congress should significantly expand funding for biomedical Manufacturing USA centers, including expanding funding for NIIMBL as well as establishing other centers addressing related manufacturing technology challenges.** In addition, **federal funding should be ongoing and not sunset.** No other nation with similar industry-university-government precompetitive research centers sunsets funding for successful centers.

In addition, **Congress should fund NSF to expand support to university-industry research centers working on biopharma production technology and potentially establish new centers.** For example, the Novartis-MIT Center for Continuous Manufacturing is a partnership launched to develop continuous production technology.<sup>239</sup> At the same time, **Congress should increase funding for NSF’s Division of Engineering and target much of the increase to the Chemical Process Systems Cluster and Engineering Biology and Health Cluster.**<sup>240</sup> Unfortunately, between 2018 and 2019, Congress

increased the engineering division's budget by just 1 percent, compared with the overall NSF budget by 3 percent.

In addition, **the administration should encourage the creation of the biopharma equivalent of the Semiconductor Research Corporation**, a public-private consortium that, among other things, works on a long-term semiconductor technology roadmap. **Industry should collaborate on such a production technology innovation roadmap, and the federal government should match their funding to research institutes and universities on a dollar-for-dollar basis.** For example, some firms have their own roadmaps (e.g., GlaxoSmithKline's manufacturing technology road map, is focused on the use of continuous techniques).<sup>241</sup>

At the same time, **Congress should establish an investment tax credit for new manufacturing facilities and equipment in the United States.** This could be structured like the Alternative Simplified R&D Credit with a credit for all investment about 50 percent of annual average investments over the prior 3 to 5 years. This could be targeted to biopharmaceutical firms or made available to all manufacturers. If there are fiscal concerns, the incentive could be time-limited to 10 years to spur significant reinvestment in the United States, including in continuous process technologies for drug production.

### Invest in Biomedical Manufacturing Talent

At the same time, there is need for more and better talent for biomedical manufacturing. The focus on talent in the industry has been on the scientists who can develop drugs, and less on the engineers and technical workers that can design and run complex production systems. As one study finds:

The lack of a biomanufacturing workforce that is well trained in [current good manufacturing procedures and analytics] and that could populate clinical and industrial manufacturing settings is seriously hampering the progress and translation of cell therapies. Significant investment in developing such a workforce—both at the level of 2-year community or technical colleges or standard 4-year universities—is critically needed.<sup>242</sup>

Congress should take several steps. **Congress should expand the Manufacturing Engineering Education Program from its current \$15 million annual funding.** In its FY 2021 budget request, DOD asked for Congress to at least double the program funding.<sup>243</sup> Further, **Congress should direct DOD to develop a competition for biomedical manufacturing programs.**<sup>244</sup> In addition, **Congress should expand funding for NSF's Advanced Technical Education program and target the funds to the development of centers focused on industry skill needs.**

### Creative Incentives for Domestic Production

If the United States is to expand domestic production, Congress will need to expand incentives for companies to invest in the United States. **Congress should task the administration with developing a national medical products strategy that would identify key vulnerabilities in biopharmaceutical and medical-product supply chains and develop solutions, where appropriate, to encourage reshoring and promote greater levels of domestic manufacturing at home.**

At the same time, **Congress should create the equivalent of the CHIPS Act and American Foundries Act, legislation to support the expansion of U.S. semiconductor production.**<sup>245</sup> Both bills provide a



model that can and should be used for the biomedical industry. In particular, Congress should allocate at least \$5 billion a year to be provided to states (matched at least with 50 cents in state funding for every \$1 dollar in federal funding) to provide incentives for the establishment of new biomedical production facilities in the United States.

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Finally, **Congress should restore the tax credit for biopharma production in Puerto Rico and other U.S. territories.** At one time, many drug companies produced critical drugs and active pharmaceutical ingredients in Puerto Rico in part because of Section 936 of the tax code, which released pharmaceutical manufacturers from taxes on profits made in Puerto Rico and other U.S. territories.<sup>246</sup> But when that provision ended in 2006 not only did it devastate the Puerto Rico economy, it led to a rush of factories moving to China, many induced by generous government incentives over there.<sup>247</sup>

### Reform Regulations of Biomedical Production

Changing biopharma production technology is not only expensive and complicated, it requires approval by the FDA. As part of its effort to assure the safety of marketed drugs, the FDA heavily regulates the manufacturing processes used to produce them. Companies seeking approval for a new drug are hesitant to put forward new manufacturing processes the FDA has not already approved in another context. Once manufacturing has begun, the FDA must certify any changes to a previously approved process. In part, as a result, the pharmaceutical industry has not seen the dramatic improvement in quality and efficiency that other industries have experienced. FDA Center for Drug Evaluation and Research Director Janet Woodcock recognized these challenges in her recent congressional testimony, observing:

The adoption of advanced manufacturing technologies may pose a challenge to the current regulatory framework, because most regulations were developed based on traditional batch manufacturing methods under a unified pharmaceutical quality system. As a result, FDA has launched an effort to identify and implement needed changes in the regulatory structure.<sup>248</sup>

As noted, the FDA's Emerging Technology Program, launched in late 2014, advances the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other relevant stakeholders.<sup>249</sup> This is an important program that the FDA should continue to improve on. And, as Director Woodcock noted, the FDA should continue to reduce regulatory barriers to investing in biopharma production in the United States. **Congressional policymakers and the next administration should continue to work with the FDA on these issues, and streamline and accelerate the FDA's capacity to evaluate and approve innovative new pharmaceutical manufacturing processes.**

### More Aggressively Contest Foreign Biopharmaceutical Mercantilism

The United States would have a larger share of global biopharmaceutical innovation and production if firms in the United States enjoyed a level global playing field. One problem, as noted, is that foreign nations continue to free-ride off U.S. investments in biomedical innovation by failing to pay their fair share for innovative pharmaceuticals. Thus, **a key objective of U.S. trade**

**policy should be prevailing on America's trade partners to appropriately value innovative medicines.**

To its credit, the USTR's Office has recognized the importance of "pressing trading partners to appropriately recognize the value of innovative medicines."<sup>250</sup> An important success came in the updated U.S.-Korea Free Trade Agreement (KORUS), which obliged Korea to appropriately value innovative medicines and provide fair and nondiscriminatory treatment of pharmaceutical products. USTR has also raised concerns with Japan as part of the U.S.-Japan Economic Dialogue "to ensure transparency and fairness and address other concerns with respect to pharmaceutical pricing and reimbursement policies."<sup>251</sup> Congress has a platform to articulate America's priorities in trade agreements with partner nations through TPA, which is due for renewal before July 1, 2021.<sup>252</sup> **Congress should use the opportunity of TPA renewal to affirm that a key priority of U.S. trade policy should be that America's trade partners pay their fair share for innovative drugs.**

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**U.S. trade policy needs to resist the mistaken view that holds that IP is not a trade policy issue.**

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In addition, **U.S. trade policy needs to resist the mistaken view that holds that IP is not a trade policy issue.** It is. Nations not being able to pilfer U.S. IP through weak laws or lack of enforcement is no different than subsidizing their exports or putting in place high import tariffs. As such, it is important that future trade agreements include strong provisions for data exclusivity. Providing for 12 years of data exclusivity for the clinical trial data that validates the safety and efficacy of innovative biologic drugs has been an important factor in the success of American biologics innovation. Accordingly, it's appropriate that the United States has sought high standards in its trade agreements for partner nations to implement similarly robust periods of data exclusivity for innovative biologic drugs. Lamentably, in the final negotiations toward the Trans-Pacific Partnership (TPP) agreement, the United States acceded to a regime providing at minimum five years and at most eight years of data exclusivity protection.<sup>253</sup> And when the Trump administration withdrew the United States from the TPP, the remaining 11 nations, which proceeded to complete the CPTPP agreement, stripped out the provision entirely. Likewise, a last-minute political compromise to get the USMCA FTA through Congress saw biologics-data exclusivity provisions get excised at the eleventh hour.<sup>254</sup> Twelve years of data exclusivity is the standard enshrined in U.S. law because it's the standard that facilitates robust biologics innovation. U.S. trade policy should advance this standard not just because it's U.S. law, but because in the trade agreements the United States enters it should be doing so with the mindset of creating the conditions in which life-sciences innovation in the United States, and in partner nations, can flourish to the greatest extent possible, for the interest of citizens and patients not just in those nations but across the world. Accordingly, it is worrisome that in recent congressional testimony, USTR Robert Lighthizer suggested he might be willing to accept shorter biologics data exclusivity terms in future U.S. FTAs.<sup>255</sup> **At a minimum, U.S. administrations should continue to seek at least 10 years of data exclusivity in FTAs, including the FTA currently being negotiated with the United Kingdom and also the CPTPP, which the next presidential administration should seek for the United States to join.**

Cross-border data flows represent a key component of the modern global economy. As described in appendix B, the ability to transmit science- and health-related data across borders is important in facilitating biopharmaceutical innovation, combatting the spread of diseases such

as the coronavirus, and improving global public health. **As such, USTR should continue to contest countries' data localization practices and restrictions on genomics-data movement as well as promoting rules, such as in the USMCA, that promote open data flows and proscribe data localization measures. In particular, U.S. policy should promote the development of an interoperable, integrated global digital health framework,** supporting the many firms and research organizations involved in digital health that rely on the Internet, the free flow of data, and centralized IT facilities to easily, cheaply, and reliably access data, patients, and health care providers around the world.<sup>256</sup>

Finally, this report documents (appendix B) the wide range of foreign innovation mercantilist practices deployed in the life-sciences sector, including discriminatory preferences, restricted market access, export bans and restrictions, efforts to undermine IP rights such as through compulsory licensing or IP theft, and failing to adequately value innovative medicines. **USTR must continue to comprehensively document and aggressively contest these unfair trade practices.** One instrument that could help in this regard would be for **USTR to produce an annual Global Mercantilist Index that comprehensively documents and ranks trade barriers imposed by America's trading partners.** USTR's Special 301 Report provides an annual review of countries that maintain inadequate IP protections and enforcement mechanisms, and its National Trade Estimate Report on Foreign Trade Barriers provides an effective inventory of significant foreign barriers to U.S. exports and investment, but ITIF's proposed Global Mercantilist Index would comprehensively identify all of the innovation mercantilist policies of America's trading partners and rank the worst offenders.<sup>257</sup>

## CONCLUSION

The United States leads the world in life-sciences R&D and innovation, but as recently as 1990 that was not the case. The evolution of U.S. life-sciences innovation leadership over the past three decades is a direct result of conscientious and intentional policy choices designed to stimulate private-sector innovation. However, that leadership position must be continually curated and stewarded, especially as other nations implement ever-more-aggressive policies to bolster their nations' life-sciences competitiveness, not only in production but also innovation.

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The federal government should continue to improve its policy environment supporting life-sciences innovation, including continuing to increase funding for NIH and eschewing draconian drug pricing systems. And it should put in place new policies, including to expand biopharma production domestically. The goal should not be complete self-sufficiency. This is neither realistic nor beneficial. However, the goal should be for the United States to expand domestic production to the point where it no longer runs a trade deficit.

Biopharmaceutical enterprises in the United States have produced life-saving and life-improving drugs that contribute greatly to global social welfare; effective policies can help ensure that America's biopharmaceutical innovation and production engine continues to flourish into the future.

## APPENDIX A: COUNTRIES PROACTIVELY BOLSTERING THEIR LIFE-SCIENCES INNOVATION SYSTEMS

A number of competitor nations have introduced sophisticated strategies to bolster the competitiveness of their life-sciences innovation systems, as the following section elaborates, with case studies of several countries/regions, including China, the European Union, Japan, Singapore, Sweden, and the United Kingdom.

### China

For over a decade, the Chinese government has targeted biopharma as a key industry for development.<sup>258</sup> The sector was first targeted in “The Guidelines for the Implementation of the National Medium- and Long-term Program for Science and Technology Development (2006–2020),” and associated implementing 11th Five-Year Plan, which called on China to “[f]orm an advanced industrial technology system supporting the development of biotechnology drugs, establish a batch of multi-functional, bio-technical drug production bases in line with international standards, and cultivate a group of enterprises with international competitiveness.”<sup>259</sup>

China’s 12th Five-Year Plan (2011–2015) identified biotechnology as one of the country’s seven priority emerging industries, but it wasn’t really until the introduction of China’s 13th Five-Year Plan (2016–2020) that China developed a serious implementation plan for the sector, calling for biotech industry output to exceed 4 percent of GDP by 2020.<sup>260</sup> China’s State Council has called on all levels of government in China to target the industry for support, writing, “The people’s governments of all provinces, autonomous regions, and municipalities directly under the Central Government, ministries and commissions under the State Council, and their respective agencies: The Bio-Industry Development Plan is hereby printed and distributed to you, please implement it carefully.”<sup>261</sup> The Bio-industry Development Plan component set a target for biopharmaceutical sales to grow to \$1.02 trillion by 2020, at an annual growth rate of 20 percent.<sup>262</sup> The State Council noted that “[i]nnovation will be strengthened through collaboration on key R&D projects, the commercialization of pharmaceuticals, advances in medical devices, and the modernization of TCM (traditional Chinese medicine). Industry and organizational structure will be optimized through cross sectoral mergers and restructuring, trans-regional shifts, and the development of concentrated industry clusters.”<sup>263</sup>

Most recently, China’s Made in China 2025 identified 10 key industries to target, including biomedicine. It set out the following goals:

- i) Goals for 2020: Promote a large number of enterprises to achieve drug quality standards and systems that are in line with international standards, among which at least 100 pharmaceutical enterprises obtain U.S., EU, Japanese, and World Health Organization (WHO) authentication and achieve product export; according to international drug standards, develop and promote 10–20 chemical and high-end drugs, 3–5 new traditional Chinese medicines, 3–5 new biotech drugs; complete drug registration in Europe, the United States, and other developed nations; speed up the development of internationalization of domestically produced drugs; before 2020, when international patents for blockbuster drugs expire, achieve over 90 percent generics production; achieve breakthroughs for 10–15 important core and critical technologies; and begin to establish national drug innovation system and innovation team.

ii) Goals for 2025: By 2025, basically achieve drug quality standards and systems that are in line with international standards; develop chemical drugs, traditional Chinese medicine, biotech drugs focused on 10 major diseases, achieve industrialization of 20–30 innovative new drugs; 5–10 drugs with indigenous property rights receive U.S. Food and Drug Administration or EU authentication, and enter the international market; construct, improve, and support the national drug innovation system for external services, form of high-level innovation team with an international perspective, promote China’s drug internationalization development strategy.<sup>264</sup>

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**China appears to be “skating to where the puck will be” in the sense that the government is focusing more on biotechnology and biology, rather than on more traditional pharmaceuticals and chemistry.**

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In addition to the national Made in China 2025 plan, at least 19 of China’s 23 provinces have their own plan. As China’s State Council wrote in 2016:

All regions and relevant departments must fully understand the importance of promoting the healthy development of the pharmaceutical industry, strengthen organizational leadership, improve the working mechanism, and form a joint effort. All regions should formulate specific implementation plans based on actual conditions, carefully organize and implement them to ensure that all tasks are implemented. All relevant departments should promptly formulate supporting policies in accordance with the division of responsibilities and create a good environment.<sup>265</sup>

China also appears to be “skating to where the puck will be” in the sense that the government is focusing more on biotechnology and biology, rather than on more traditional pharmaceuticals and chemistry. Its 13th Five-Year Plan focuses on “genomics and other biotechnologies, networked application demonstration, and the scaling up of a new generation of biotechnology products and services, including personalized treatment and innovative pharmaceuticals.”<sup>266</sup> Some genomics-based drugs may need to be tailored by ethnicity, which would give the Chinese an advantage in developing drugs for Chinese use. China is focusing more on complex biotechnology drugs in part because that is where much of the industry is going globally. As one article noted, “China’s leading biotech companies are already aware of the need to step up their game. The novel chemical drug space may be close to saturation, but there’s still a lot to explore in the biopharmaceutical field, and that is where China has the potential to catch up with the world leaders.”<sup>267</sup>

In summary, China’s biopharma strategy appears to be focused on growing and improving its generics industry, in part by having a relatively weak IP system, and then on the basis of that growth, encouraging the generics industry to innovate more, coupled with state support of biotech start-ups.<sup>268</sup> China also expects to have robust access to international markets to sell its biotechnology exports, with 86 percent of Chinese biopharma manufacturers expecting to produce for export to the United States and the European Union in the future, compared with 25 percent that do so today.<sup>269</sup>

## European Union

The nations of the European Union have long prioritized biopharmaceutical innovation and investment as keys to economic competitiveness, though recent years have seen a number of social and political obstacles arise which challenge the success of traditional strategies.

In 2011, the European Union launched its Innovation Union policy, one of the seven flagship initiatives of the Europe 2020 strategy laying out a “comprehensive innovation approach” for Europe. The Innovation Union, containing over 30 actions points with 3 overarching goals of making Europe competitive on the world stage of science performance, removing obstacles to innovation, and revolutionizing public-private partnerships has since been replaced by new policy as dictated by former European Commissioner of Research, Science, and Innovation Carlos Moedas, in 2015. According to the European Commission today, the three current policy goals of EU research and innovation are “open innovation, open science, and open to the world.”<sup>270</sup> In an effort to promote these goals and monitor progress, the commission introduced multiple tools, including the Innovation Union Scoreboard and the Regional Innovation Scoreboard, which use a variety of indicators to categorize Member States and regions as innovation leaders, innovation followers, moderate innovators, and modest innovators. The EU also set a target of investing 3 percent of total GDP in R&D by 2020 through increasing numbers of researchers, integrating European and national research policies, and increasing mobility for researchers across state lines. As a final component of the EU’s strategy to measure and report on innovation performance, the European Commission’s Innovation Output Indicator demonstrates the extent to which innovative ideas translate to life-sciences markets and jobs and, in 2020, indicates that the EU is “falling short in innovation output compared to the United States and Japan”<sup>271</sup>

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Multiple social and political changes in Europe have made the path to successful biopharmaceutical policy more complicated for the nations of the European Union. With aging and, in some parts, declining populations, the EU has needed to reevaluate current social welfare and health-care systems for their effectiveness in light of demographic changes. Likely increases in social care expenditures to address the needs of an older population will require the diversion of resources originally devoted to research and innovation in the life sciences. As evidenced by Brexit, reductions in freedom of movement throughout Europe have translated to declines in research and innovation, as significant numbers of EU scientists have emigrated. A lack of available talent in the EU is particularly foreboding for the state of U.K. biopharma, as 53.5 percent of U.K. international scientific collaborations are with EU nations.<sup>272</sup> More immediately, the impact of the coronavirus pandemic has been substantial upon the availability of resources for innovation, even as life-sciences research has come to the forefront of many nations’ agendas.

Europe undoubtedly possesses a strong research foundation and the resources needed to achieve and maintain competitiveness in the biopharmaceutical industry. Horizon Europe, Europe’s flagship R&D funding program going forward, intends to invest €100 billion (\$113 billion) over the seven years from 2021 to 2027.<sup>273</sup> Notably, it will include the European Innovation Council, funded with €10 billion to “turn Europe’s scientific discoveries into businesses that can scale up



faster.”<sup>274</sup> In the prior Horizon 2020 program, 9.7 percent of its budget had gone to the “health and wellbeing” category, focusing on “investment in health research and innovation ... to give doctors the tools they need for more personalized medicine [and] step up prevention and treatment of chronic and infectious diseases.”<sup>275</sup> With 16 of the world’s top-50 universities for life sciences, half of the world’s biotech companies centralized in France, Germany, Switzerland, and the United Kingdom, and massive potential in emerging treatment areas leveraging technologies such as antisense, viral vectors, and siRNA, Europe is a capable and a competitive player in life-sciences innovation. That said, where Europe excels at early innovation in terms of research publications, it falters in later-stage innovation indicators such as high numbers of innovative candidates and drug approvals. The United States’ patent originations triple those of Europe; China originates roughly nine times as many patents as Europe does.<sup>276</sup> Amidst uncertainty in the wake of Brexit and in the throes of a global pandemic, the EU must take practical steps toward translating scientific potential into tangible innovation.

## Japan

Japan’s biopharmaceutical competitiveness has faltered over the past decade. Japan’s share of value-added in the global pharmaceutical industry declined by 25 percent from 2001 to 2016.<sup>277</sup> The number of new chemical and biological entities Japan has introduced in five-year increments is virtually unchanged over the past three decades: Japan introduced 29 from 1997–2001, faltered to 21 from 2002–2006 and 20 from 2007–2011, and barely bounced back to 32 from 2012–2016.<sup>278</sup> And whereas Japan accounted for 23 percent of such innovations from 1997–2001, it accounted for just 13 percent from 2012–2016, a decline in share of 56 percent. The country has gone from having balanced trade in pharmaceutical products in 2001 to a trade deficit today.<sup>279</sup> Japan now accounts for only 3 of the world’s 26 largest life-sciences firms. And while business R&D investment in the life-sciences remains strong, Japan’s government invests just one-sixth the amount in life-sciences R&D that the United States does.

Several specific challenges have confronted Japan’s life-sciences innovation system. Japan has long had difficulties with translational research and technology transfer, and has suffered from weak cooperation between public and private research entities. The country faces high and rising costs of clinical trials and difficulty in getting patients registered for them. Further, Japan has not harmonized with international guidelines to facilitate Japanese participation in regional clinical trials. Because of this, Japan has significantly trailed the United States and Europe in developing an expedited regulatory pathway for approval of innovative medicines.

In 2018, Japan significantly revised its Pharmaceutical Price Maintenance Premium (PMP), the program responsible for ascertaining reimbursement levels the government pays for innovative medicines.<sup>280</sup> But, in part because the system fails to conduct a science-based evaluation of new medicines, many best-selling global products have been deemed not innovative under the new criteria and consequently stripped of their PMP eligibility. In fact, according to Japan’s Ministry of Health, Labor, and Welfare (MHLW), approximately 30 percent of patented medicines no longer qualify for the PMP. Japan is also piloting a Health Technology Assessment system that seeks to assess the value of innovative medicines and technologies. While such an approach isn’t unreasonable, a particular concern is that it does not include the societal value of innovative medicines.

In response to Japan's faltering life-sciences competitiveness, in 2014, the country introduced the "Sakigake package" which sought to accelerate drug and device approvals and cut review times. Legislatively, these changes were enacted through the PMD—Pharmaceutical and Medical Devices—Act.<sup>281</sup> The PMD Act's acceleration of regulatory approvals for some drugs and devices played an important role in subsequently triggering a number of partnerships, licensing deals, and research collaborations in Japan with international companies.

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**Japan has long been a key biopharmaceutical innovator, but comprehensive policy reforms—particularly with regard to drug pricing and the willingness to pay for innovative medicines—are needed if it's going to keep pace with the United States, European countries, and China.**

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In 2015, the country took another step by introducing its *Japan Vision: Health Care 2035: Leading the World Through Health*, a long-term policy vision from the health ministry.<sup>282</sup> The strategy focuses on three prongs. The first focuses on increasing longevity and quality of life for Japan's rapidly aging society; the second on improving the country's biotech and IT ecosystem, in particular leveraging health care IT such as telemedicine and using AI for medical data analysis; and the third on advancing innovation in specific areas associated with aging, including regenerative medicine, diabetes, and dementia.<sup>283</sup> Other priorities in the strategy included developing a national platform to support clinical trials, further speeding up drug approval timelines, and introducing incentives that promote the development of orphan drugs.

More recently, Japan has tried to enhance the quality of its medical data environment as a platform supporting biopharmaceutical innovation. In 2019, a legal revision allowed medical data to be anonymized and provided for new uses. Japan's Medical Information Database holds health data for more than 127 million subscribers, and the government, industry, and academia have been able to tap into the database to get better real-world data evidence for clinical trials, and enhance the efficiency and speed of pharmacovigilance (monitoring the safety of drugs post-approval) efforts. As Akira Miura, director of the Economic Affairs Division, Health Policy Bureau at MHLW, noted, "Japan's promotion of data and regulatory reform together accelerate drug development, which leads to faster patient access."<sup>284</sup> Japan has long been a key biopharmaceutical innovator, but comprehensive policy reforms—particularly with regard to drug pricing and the willingness to pay for innovative medicines—are needed if it's going to keep pace with the United States, European countries, and China.

## Korea

In May 2019, Korea introduced its "Innovative Strategy on the Bio-health Industry," a holistic strategy seeking to create a comprehensive, innovative ecosystem ranging from technology development, approval, production, and export.<sup>285</sup> (Korea defines its "Bio-health Industry" as comprising manufacturing industries, including medicines and medical devices, and "the service industry of health management.") The strategy increased the government's annual R&D investment in the sector to KRW 4 trillion (\$3.3 billion), up from KRW 2.6 trillion (\$2.15 billion) annually; increased financing for the industry from state banks by KRW 2 trillion (\$1.7 billion) over the next five years; established a big data strategy to support the sector's development, including the introduction of five new big data platforms; and committed to improve its regulatory approach to match those of global leaders.<sup>286</sup> The Korean government established a goal of achieving a three-fold increase in Korea's share of the global bio-health industry, from 2



percent to 6 percent; reaching \$50 billion in exports from the sector, up from \$14.4 billion today; and creating 300,000 new jobs. The strategy also includes a “National Bio Big Data” initiative that will enroll up to one million people to be utilized in R&D on personalized new drugs and medical technology by 2029. It further includes a “master plan” to nurture professionals in the bio-health field in coordination with industry demand, and creates a cooperation mechanism for open innovation between leading companies, start-ups, and venture firms.

## Singapore

Singapore has worked for over two decades to transform itself into a global hub for biomedical R&D and innovation. Biomedical research from Singapore has contributed greatly to improving the world’s understanding of cancer, eye diseases, neuroscience, metabolic diseases, and infectious diseases, among others.<sup>287</sup> Singapore has invested significantly in the sector, launched ambitious initiatives to attract world-class scientific talent, and instituted policies to encourage translation of basic research into commercially viable health care technologies.<sup>288</sup>

Notably, in 2003, Singapore established its “Biopolis,” which provides dedicated research and residential facilities and co-locates public research institutes with corporate laboratories in order to foster collaboration.<sup>289</sup> As Dr. Benjamin Seet, executive director of the Biomedical Research Council at the Agency for Science, Technology and Research (A\*STAR), a public research and technology organization that funds R&D directed toward economic outcomes in Singapore, noted, “After working for years to build our biomedical talent and infrastructure, Singapore’s public research institutes and universities spawned nearly two hundred new biotech and healthcare technology companies in the past few years.” Between 2015 and 2018, 32 local biotech start-up firms were set up, double the number incorporated between 2012 and 2014. Nearly one-quarter of the 79 home-grown biotech firms operating in Singapore last year were spin-offs from A\*Star.<sup>290</sup>

Overall, the strengths of Singapore’s biopharmaceutical innovation system include robust IP rights and enforcement; sustained and growing government investment in human skills, technology transfer, and advanced manufacturing capacity through industry partnerships; and an attractive clinical trial environment. Singapore has also cultivated a biopharmaceutical regulatory framework that’s viewed as enforcing rigorous standards, approving innovative drugs timely and efficiently, and embracing international standardization and platforms for cooperation and capacity building.<sup>291</sup>

## Sweden

Sweden provides an interesting case study for biopharmaceutical competitiveness within the context of the European Union. Home to pharmaceutical giants such as AstraZeneca, the former Pharmacia, Novo Nordisk, and Lundbeck, the Swedish life-sciences industry represents an important player in the global therapeutics market. In a 2014 EY report on Nordic life-sciences sectors, researchers noted, “The majority of the compounds of the Nordic biotech pipeline are generated in Sweden and Denmark, which together contributed almost 80% of the total pipeline in 2013.”<sup>292</sup> Despite faring better than other industries and its neighbors after the 2008 financial recession, Sweden’s biotech and medtech industries struggled to recover capital in subsequent years and increasingly began to seek public financing through IPOs. The reduced size of these deals post-recession, however, meant that Sweden’s share of innovation capital—

that is, equity capital raised by companies with revenues of less than \$500 million—declined from 2010 through 2014.<sup>293</sup> 2013 also saw a number of major mergers and acquisitions deals in the Swedish life-sciences industry, with an aggregated deal value of over \$4 billion.

Equipped with already-strong life-sciences and ICT industries, Sweden has enjoyed the benefit of being a natural choice for VC funding. Between 2012 and 2017, 35 percent of VC investments in Sweden were made in the life-sciences sector, which in 2017 accounted for over SEK 836 million (\$90.8 million).<sup>294</sup> Paired with a favorable market and an increased demand for new markets such as China, Sweden’s life-sciences sector saw an increase in net turnover by 27 percent, along with a 15 percent increase in exports between 2014 and 2016.<sup>295</sup>

Moving forward, Sweden has maintained its position at the forefront of life-sciences innovation by responding to global trends. It has developed a strong national and regional eHealth infrastructure, established collaboration and cooperation between suppliers and the public sector, and created space for industry leaders to innovate with apps such as AstraZeneca’s E-Brilique, which makes care and medical advice more accessible for patients with myocardial infarctions.<sup>296</sup> Swedish companies have harnessed Big Data with initiatives such as Elekta’s development of a global cancer informatics database and AstraZeneca’s academic research partnership with Uppsala University to produce a massive and long-term observation study of chronic obstructive pulmonary disease (COPD). Recent investments made by large pharmaceutical companies such as AstraZeneca and GE Healthcare have yielded advanced manufacturing facilities on home turf, further bolstering production capacities and an international reputation for biopharma leadership. Finally, industry players have shown a willingness to invest in orphan drug development despite the difficulty of realizing returns, justifying the move with backup plans of revised remuneration models to share risk. Today, Sweden maintains its position as the largest pharmaceuticals market in the Nordics region and the sixth-largest in the EU, exporting principally to Germany, China, and the United States.<sup>297</sup>

## United Kingdom

Following the financial crisis of 2008, the United Kingdom overcame a massive budget deficit and a perceived lack of commitment to scientific research with the December 2011 implementation of the *Strategy for UK Life Sciences*, a plan calling for new research investments, reforms to existing tax, regulatory, and talent policies, and an overarching goal of becoming the “global hub for life sciences in the future.”<sup>298</sup> Among policies implemented were considerable investments in existing life-sciences-focused research councils, including the Medical Research Council and the Biotechnology and Biological Sciences Research Council, as well as financial support of new research, treatments targeted at specific populations, and small to medium-sized enterprises in the field. Beyond investment, the United Kingdom made policy adjustments with life-sciences competitiveness in mind, reducing corporate taxes on profits from new IP such as patents through “patent boxes,” introducing an “above the line” R&D tax credit, and improving the efficiency of its regulatory drug approval system.<sup>299</sup> The nation also introduced a cross-sector Office for Life Sciences, bringing together the Ministries of Health and Business with the common goal of propelling biopharma forward.

The UK’s 2011 *Strategy* was met with mixed results; while ventures such as the Biomedical Catalyst Fund accelerated numerous medical research projects by matching private funding, other projects failed to deliver on their objectives or, in some cases, even come to fruition. The

Innovation Scorecard, a tool intended to promote understanding of British National Health Service performance and effectiveness for patients making choices about their service providers, was criticized for being underdeveloped and undetailed.<sup>300</sup>

In order to maintain its attractiveness as a global biopharmaceutical hub even after withdrawing from the EU, the United Kingdom has enacted policies intended to align with EU regulations. The Life Sciences Sector Deal's commitment to increase the uptake of innovative medicines and the renegotiation of the Pharmaceutical Pricing and Regulation Scheme (now the Voluntary Pricing Access Scheme) sent messages of encouragement to industry players through increased transparency of approval processes and greater attention to the specific needs of complex specialized medicines from the National Institute for Health and Care Excellence, which elected to maintain its existing "cost-effectiveness threshold."<sup>301</sup> Parliament is currently debating the Medicines and Medical Devices Bill, which aims to ensure growth and increased availability of innovative medicines and research by reducing bureaucratic red tape in clinical trials and licensing processes, and increasing the number of professions able to prescribe and supply medicines.<sup>302</sup>

## APPENDIX B: FOREIGN INNOVATION MERCANTILISM

While many nations are trying to bolster their competitiveness in the biopharmaceutical industry through effective strategies and policies, many are also trying to compete through innovation mercantilist practices that distort trade and competition on market-based terms, thus harming enterprises and industries trying to compete on a legitimate basis. As the following section shows, such distortive policies can include free-riding by undervaluing innovation; export restrictions on pharmaceutical or medical products; data localization policies that restrict the cross-border flow of health information; IP policies—such as compulsory licensing, weak IP regimes, and IP theft—that fail to respect foreign IP rights; and discriminatory foreign government policies designed to support countries’ own biopharma industries.

### Foreign Nations Undervaluing Innovation

The United States provides an environment where innovative life-sciences companies can earn sustainable returns on their investments in life-sciences innovation. But this has created a situation whereby other nations can free-ride off U.S. investments in life-sciences innovation by failing to pay their fair share for innovative medicines. As Goldman and Lakdawalla wrote in “The Global Burden of Biomedical Innovation,” “America clearly contributes more to pharmaceutical revenue, and hence for new drug development, than its income and population would suggest.”<sup>303</sup> In fact, U.S. consumers spend roughly three times as much on drugs as their European counterparts, and 90 percent more as a share of income.<sup>304</sup>

In its report, “How National Policies Impact Global Biopharma Innovation: A Worldwide Ranking,” ITIF ranked 56 nations on the extent to which their scientific research, drug pricing, and IP policies contribute to global biopharma innovation, and assessed the extent to which nations impose price reductions on the sale of pharmaceutical products. Nations can enact price controls on pharmaceuticals either directly or indirectly based on their national structure for health care provision.

Two studies provided a means of grouping countries based on whether their citizens pay high, moderate, or low prices for pharmaceuticals relative to their country’s average income levels. First, OECD has compared price levels for pharmaceuticals against standardized economy-wide price levels. To compare across countries, prices were adjusted by the spending power of countries’ domestic currency relative to the U.S. dollar. A theoretical basket of pharmaceuticals and general products was developed to perform cross-country comparisons. The basket contained a mix of 75 percent original drugs and 25 percent generics. The study assessed whether consumers in OECD countries were overpaying or underpaying for their pharmaceuticals relative to day-to-day goods and services.<sup>305</sup> Second, a paper examining differential pricing of pharmaceuticals worldwide compared net-sales data of drug purchases to a theoretical equitable price weighted by gross national income levels and purchasing price parity. Through this framework and across all national incomes, certain countries were found to pay more than an “equitable” price for drugs, while others pay less.<sup>306</sup>

ITIF thus ranks countries based on whether they impose low, moderate, or high levels of forced price reductions on pharmaceutical sales. (See table 7.) The table shows that 9 countries exhibit a limited degree of forced price reduction for pharmaceutical drugs, while 11 nations exhibit high levels of forced price controls.

**Table 7: Countries' extent of pharmaceuticals price controls (sorted by extent of reduction and alphabetically)<sup>307</sup>**

Country	Extent of Pharmaceuticals Forced Price Reductions	Country	Extent of Pharmaceuticals Forced Price Reductions
Argentina	Low	Lithuania	Moderate
Hong Kong	Low	Malaysia	Moderate
Indonesia	Low	Netherlands	Moderate
Israel	Low	New Zealand	Moderate
Mexico	Low	Peru	Moderate
Singapore	Low	Philippines	Moderate
Switzerland	Low	Poland	Moderate
Taiwan	Low	Portugal	Moderate
United States	Low	Romania	Moderate
Austria	Moderate	Russia	Moderate
Belgium	Moderate	Slovak Republic	Moderate
Brazil	Moderate	Slovenia	Moderate
Bulgaria	Moderate	South Korea	Moderate
Canada	Moderate	Sweden	Moderate
Chile	Moderate	Turkey	Moderate
Colombia	Moderate	Ukraine	Moderate
Costa Rica	Moderate	Vietnam	Moderate
Czech Republic	Moderate	Australia	High
Estonia	Moderate	China	High
Finland	Moderate	Denmark	High
Germany	Moderate	France	High
Greece	Moderate	India	High
Hungary	Moderate	Ireland	High
Iceland	Moderate	Norway	High
Italy	Moderate	Spain	High
Japan	Moderate	Thailand	High
Kenya	Moderate	South Africa	High
Latvia	Moderate	United Kingdom	High

As noted, if peer nations relaxed price controls and paid more for innovative medicines, it would bolster global life-sciences innovation for the benefit of humanity. For instance, research conducted by the U.S. Department of Commerce found that moving to market-based systems would add billions of dollars of R&D for new medicines, and would result in lower prices and benefit patients globally through increased competition. Precision Health Economics found that if government price controls in non-U.S. OECD countries were lifted, the number of new treatments available would increase by 9 to 12 percent by 2030, equivalent to 8 to 13 new drugs in that year.<sup>308</sup> Likewise, as Goldman and Lakdawalla wrote in “The Global Burden of

Biomedical Innovation,” “While American subsidies to innovation provide much-needed philanthropy to poor countries, patients in richer countries outside the United States would benefit longer-term if they financed a greater share of drug discovery.” The authors estimated that if European prices were 20 percent higher, the resulting increased innovation would generate \$10 trillion in welfare gains for Americans, and \$7.5 trillion for Europeans over the next 50 years.<sup>309</sup> As they wrote, “If higher prices in Europe spurred just a few innovators to develop effective dementia treatments [for instance], the additional prescription spending would be worth it.”

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## **Export Restrictions**

The coronavirus crisis has highlighted the importance of and significant value international supply chains have generated for the global economy, particularly with regard to the development of lowest-cost/highest-value-added advanced-technology products, including biopharmaceuticals and medical supplies.<sup>310</sup> Yet export restrictions disrupt global supply chains and innovation processes while harming companies and placing patients’ lives at risks, as the coronavirus crisis has also brought into stark relief. For instance, on March 3, 2020, India announced that it would stop exporting 26 drugs and drug ingredients, including for a wide variety of antibiotics.<sup>311</sup> Likewise, the Chinese government forced personal protective equipment (PPE) producers, including factories that produce equipment on behalf of Western companies, to sell every unit they made to the Chinese government when the COVID-19 epidemic was at its worst in China from late January through February 2020.<sup>312</sup> In April, Chinese export restrictions and customs complications left stranded in warehouses and delayed shipments of even American companies’ own Chinese-manufactured, U.S.-bound face masks, test kits, and other medical equipment that was so urgently needed. U.S. companies such as PerkinElmer, which makes coronavirus testing kits, and Medtronic, which produces ventilators, were unable to import key components and final goods needed to respond to the pandemic over a crucial period in April.<sup>313</sup>

Unfortunately, that’s just been the tip of the iceberg, as by June 2020 more than 60 countries had introduced export curbs or restrictions on medical supplies related to COVID-19 alone.<sup>314</sup> (See table 8.) Even the United States’ Federal Emergency Management Agency (FEMA) issued a temporary rule on April 10, 2020, to allocate five types of PPEs for domestic use, so that these materials may not be exported from the United States without explicit approval by FEMA.<sup>315</sup> Such export bans or restrictions distort global trade; provide other nations with a justification for introducing their own export bans in the biopharmaceutical, medical supplies, or other sectors; and should in general be avoided by policymakers.

**Table 8: Countries introducing international export restrictions on COVID-19-related products and technologies<sup>316</sup>**

Country			
Albania	Cyprus	Latvia	Saudi Arabia
Algeria	Czech Republic	Lebanon	South Africa
Argentina	Ecuador	Libya	South Korea
Armenia	Egypt	Malaysia	Spain
Australia	Estonia	Moldova	Switzerland
Azerbaijan	France	Morocco	Syria
Bahrain	Hungary	Nepal	Taiwan
Belarus	India	Norway	Thailand
Belgium	Indonesia	Oman	Turkey
Brazil	Israel	Pakistan	Ukraine
Bulgaria	Jordan	Paraguay	United Arab Emirates
China	Kazakhstan	Peru	United States
Colombia	Kenya	Philippines	Uzbekistan
Costa Rica	Kuwait	Poland	Vietnam
Côte d'Ivoire	Kyrgyzstan	Romania	Zimbabwe

## Barriers to Health Data and Information Flows

Just as in virtually every other sector of the economy, data increasingly provides a platform for biopharmaceutical innovation, a dynamic that has only been accelerated with the advent of more-sophisticated tools such as AI—which has shown tremendous potential to identify biomarker disease targets in the human body or to model the morphology of pathogens such as cancer or coronaviruses in the search for treatments.<sup>317</sup> But just as diseases such as Ebola, malaria, and COVID-19 don't stop at nations' borders, health care researchers and providers need to be able to effectively move data about these and other health challenges across borders in order to prevent and treat them.<sup>318</sup> That's why countries need to implement an international data governance framework that permits the movement of relevant health data and services across borders while preserving patient anonymity and privacy.<sup>319</sup>

For instance, China has one of the widest sets of data localization policies in the world, including for personal, financial, mapping, and health data.<sup>320</sup> In May 2019, China enacted rules that not only force firms to store genomic data locally, but also mandate that all processing has to take place locally and by local firms—as foreign organizations are explicitly prohibited from managing Chinese genomic data.<sup>321</sup> In May 2020, China fast-tracked a new law (which it hopes to enact by year-end 2020) ostensibly designed to help prevent infectious diseases and other “biological threats,” but which would potentially restrict all data resulting from cross-border scientific collaborations from leaving China without government approval—and without the partnering Chinese entity retaining some sort of rights over any technologies eventually developed.<sup>322</sup>

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Unfortunately, a number of additional countries have enacted or proposed data localization requirements that affect health data and related services, including the following:

- In 2012, Australia enacted the Personally Controlled Electronic Health Records Act, which requires personal health records be stored only in Australia.<sup>323</sup>
- Two Canadian provinces, British Columbia and Nova Scotia, have implemented laws mandating personal data held by public bodies such as schools, hospitals, and public agencies must be stored and accessed only in Canada, unless certain conditions are fulfilled.<sup>324</sup>
- India's draft data protection bill permits the government to classify any sensitive personal data as critical personal data and mandate its storage and processing exclusively within India. This highlights the potential for localization, which would be consistent with both India's recent decision to require localization for payments data and its potential application for other types of data.<sup>325</sup> Furthermore, for other types of personal data, firms must store a copy in India (known as data mirroring) before transferring data overseas (but only under certain conditions).
- In 2015, Russia enacted a Personal Data Law that mandates data operators that collect personal data about Russian residents must “record, systematize, accumulate, store, amend, update and retrieve” data using databases physically located in Russia.<sup>326</sup>
- Countries also enact de facto barriers to transfers of health and genomic data that make it harder and more expensive, if not impractical, for firms to transfer health-related data overseas. For example, South Korea and Turkey require firms to get explicit consent from residents in order to transfer sensitive data such as genomic data overseas.<sup>327</sup>

By erecting barriers to the exchange of medical information—even anonymous data—countries' protectionist policies harm not only their own residents, but also people around the world, all of whom benefit from advances in medical research that may be possible from the aggregation and analysis of health and genomic data.



## Weakening Intellectual Property Rights

As noted previously, robust IP rights represent a foundational enabling pillar for life-sciences innovation. As ITIF's Innovate4Health series—which has profiled over 40 case studies of life-sciences innovators from developing nations and whose histories tell a story of how IP rights facilitated their innovation efforts—has shown, strong life-sciences IP rights are as important in developing countries as they are in developed countries.<sup>328</sup> Unfortunately, some countries have taken steps that have weakened their IP environments, which is detrimental both to the cause of life-sciences innovation by entrepreneurs in their own countries, as well as to the prospect of new-to-the-world drugs being introduced rapidly in their own nations. Such policies include compulsory licensing, patent regimes with expanded utility tests making it difficult to secure IP rights, and the outright theft of foreign IP.

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### Compulsory Licenses

Article 30 of the Trade-related Aspects of Intellectual Property (TRIPS) Agreement states that governments may provide limited exceptions to exclusive patent rights, so long as the measures do not unreasonably prejudice the legitimate interests of rightsholders or conflict with the normal exploration of a patent. TRIPS Article 31 articulates the conditions under which countries can introduce compulsory licenses—a government order permitting the use by government or third parties of the subject matter of a patent without the authorization of the patent holder—stating that compulsory licenses must only be authorized on a case-by-case basis, be limited in scope and duration, be nonexclusive, and that any licensee must pay adequate compensation to the rights holder based on the patent's economic value.<sup>329</sup> The Doha Declaration on the TRIPS Agreement and Public Health Use permitted World Trade Organization members nations, in accordance with specified and limited procedures, to issue compulsory licenses to export pharmaceutical products to countries that cannot produce drugs for themselves. Use of compulsory licenses is permitted by TRIPS only after efforts have been made to acquire a technology on commercial terms through voluntary licensing. Voluntary licenses can only be bypassed with the issuance of compulsory licenses under conditions of national emergency or other circumstances of extreme urgency.<sup>330</sup> Nonetheless, some countries have tried to use compulsory licensing as an industrial policy to stimulate domestic generic pharmaceuticals manufacturing. But issuing compulsory licenses on rightsholders' legitimate IP rights forces the involuntary disclosure of their hard-won technology or knowledge, and undermines a nation's own IP and innovation environment.

Unfortunately, an increasing number of countries have considered or are issuing compulsory licenses. For instance, since 2004, Indonesia has issued compulsory licenses on nine patented pharmaceutical products, and revisions to the country's Patent Law in 2016 gave the Indonesian government the ability to grant compulsory licenses on broad public interest grounds.<sup>331</sup> On March 18, 2020, Israel issued a compulsory license permitting the generic manufacture of AbbVie's Kaletra, an anti-HIV/AIDS drug, without consultation with the patentee.<sup>332</sup> Peru's Congress has introduced legislation that would demand issuance of a compulsory license on an innovative HIV treatment. Chile's legislature has passed multiple resolutions demanding Chile's

Ministry of Health issue a compulsory license on the hepatitis C treatment sofosbuvir, and, in 2018, the Ministry complied, issuing Resolution 399, which declared that there are public health reasons that justify issuing compulsory licenses on certain patent-protected drugs used to treat hepatitis C.<sup>333</sup> More recently, Chile's Chamber of Deputies passed a resolution calling on the country's government to declare its support for issuing compulsory licenses on patented products that could be useful in treating the coronavirus. Likewise, a commission of the Ecuadorian National Assembly passed a resolution on March 20, 2020, directing Ecuador's health minister to issue compulsory licenses on products whose availability is important to the public health response to COVID-19.<sup>334</sup> In Colombia, CL Decree 476 CL authorizes the Colombian Ministry of Health to issue compulsory licenses on COVID-19-related technologies.<sup>335</sup>

But while compulsory licenses can seem like an easy shortcut to stimulate lower-cost domestic pharmaceutical manufacturing, they inflict significant long-term damage on countries' own life-sciences innovation ecosystems, while inducing companies to refrain from or delay introducing the most cutting-edge technologies in countries, meaning policymakers are denying or delaying their own citizens' access to the latest, life-improving or life-saving medical technologies. That's because it's clear that the quality of a country's IP environment impacts the introduction of leading-edge products and technologies, including pharmaceuticals. For instance, Cockburn and Lanjouw, in their study "Patents and The Global Diffusion of New Drugs," examined 642 new drug launches in 76 countries from 1983 to 2002, finding that the speed and extent of drug diffusion was strongly associated with countries' patent (and price regulation) regimes, and that countries moving from a regime of "no product patents" to "long product-patent terms" reduced drug launch lag times by 55 percent.<sup>336</sup> Moreover, there's evidence that compulsory licenses may do little to significantly lower prices. In their report, "Compulsory Licensing Often Did Not Produce Lower Prices For Antiretrovirals Compared To International Procurement," Beall, Kuhn, and Attaran analyzed 30 compulsory licenses of HIV/AIDS retroviral drugs against 673 comparable procurements, finding, "Compulsory licensing often delivered suboptimal value compared to intl. procurement alternatives." In fact, they found that in two-thirds of cases, the HIV/AIDS retroviral drugs were acquired by compulsory licensing, with a price premium of 25 percent.<sup>337</sup>

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Clearly, in the context of the coronavirus crisis, some nations have rushed to react by calling for the issuance of compulsory licenses. But the fundamental problem with the coronavirus is not IP, it's that the world doesn't have the IP—that is, the knowledge and knowhow—to develop effective vaccines or treatments (beyond Gilead's remdesivir, which though a useful therapeutic, remains far from a cure). Instead of seeking to issue compulsory licenses, especially when many companies have said they are willing to voluntarily make coronavirus therapies available affordably or at not-for-profit costs to least-developed nations, countries should be much more focused on preparing their health-care systems to be positioned to deploy coronavirus vaccines and therapies to their populations.

## Weak Patent Regimes

TRIPS lays out standards for patentability criteria, noting that countries should make patents available across all fields of technology in accordance with the principles that the innovative technology be novel, non-obvious, and capable of industrial application. But some countries, such as Canada with its erstwhile “promise doctrine” or India with its India Patents Act, have either introduced expanded tests for utility or narrowed patentability criteria. As the USTR’s Office noted in its 2020 Special 301 report, “In the pharmaceutical sector, Section 3(d) of the India Patents Act also remains problematic. One implication of its restriction on patent-eligible subject matter is the failure to incentivize innovation that would lead to the development of improvements with benefits for Indian patients.”<sup>338</sup> Section 3(d) of India’s Patents Act holds that pharmaceutical companies have to prove significant clinical efficacy enhancements in their drugs over already-patented compounds.<sup>339</sup> India’s application of Section 3(d) of the Patents Act in the past has meant companies were not able to secure patent rights for innovative drugs in India, whereas they were able to do so in other nations. For instance, in 2013, the Indian Supreme Court rejected Novartis’s application for a patent for Glivec, its then-breakthrough anti-leukemia drug, on the grounds that the active compound in Glivec, imatinib mesylate, failed “in both the tests of invention and patentability.” This despite the fact the drug enjoyed patent protection in over 40 other countries at the time.<sup>340</sup>

In other words, the patentability standards established under Section 3(d) of India’s Patents Act—which require a demonstration of “enhanced efficacy”—erect an additional hurdle to obtaining a pharmaceutical patent in India that goes beyond the TRIPS standard that inventions that are new, involve an inventive step, and are capable of industrial application are entitled to patent protection. Moreover, this additional condition of showing “enhanced efficacy” appears to be applied only to pharmaceuticals, thus unfairly discriminating against a particular field of technology.<sup>341</sup> Not only does Section 3(d) have the effect of limiting patentability of potentially beneficial biopharmaceutical innovations, it also undermines incentives for innovation by preventing patentability for improvements which do not relate to efficacy, such as an invention relating to the improved safety of a product.<sup>342</sup> Separately, India also lacks rules to protect undisclosed testing and other data generated to obtain marketing approval for pharmaceutical and agrochemical products against unfair commercial use and unauthorized disclosure.

## Intellectual Property Theft

As noted, IP may account for as much as 80 percent of a life-sciences company’s value, making the sector extremely vulnerable to attempts to pilfer key IP related to molecular compounds or manufacturing processes. A recent PwC survey of 119 global pharmaceuticals and life-sciences CEOs found 64 percent were “concerned that an inability to protect intellectual property will hamper growth.”<sup>343</sup> Foreign IP theft costs the U.S. economy as much as \$600 billion annually.<sup>344</sup>

China is the world’s leading practitioner of IP theft. In fact, the U.S. Federal Bureau of Investigation has 2,000 active investigations tracing back to the Chinese government related to Chinese “economic espionage,” including IP theft, an increase of 1,300 percent over the past decade.<sup>345</sup> China accounts for an estimated 80 percent of all IP thefts from U.S.-headquartered organizations—one reason why, in 2018, one in five North American CEOs reported their companies experienced IP being stolen in China.<sup>346</sup> As in most technology fields, Chinese state-sponsored actors also target biopharma firms for theft of IP, including through cybertheft and

rogue employees.<sup>347</sup> For instance, Chinese agents have hacked into systems at U.S. biopharma companies, including Abbott Laboratories and Wyeth (now part of Pfizer).<sup>348</sup>

China-championed trade-secret theft is a particular challenge. In 2013, two Chinese nationals who had been employed as scientists at Eli Lilly were charged with stealing and providing trade secrets to a Chinese pharmaceutical firm.<sup>349</sup> In 2018, Yu Xue, a leading biochemist working at a GlaxoSmithKline research facility in Philadelphia admitted to stealing company secrets and funneling them to Renopharma, a rival Chinese biotech firm funded in part by the Chinese government.<sup>350</sup> In 2019, MD Anderson and Emory University both dismissed Chinese-born scientists for theft of IP.<sup>351</sup> A report to the U.S. China Economic and Security Review Commission notes Ventria Bioscience, Genentech, GlaxoSmithKline, Dow AgroSciences LLC, Cargill Inc, Roche Diagnostics, and Amgen have all experienced theft of trade secrets or biological materials perpetrated by a current or former employee(s) with the intent to sell them to a Chinese competitor.<sup>352</sup> In academia, researchers have stolen biotech information or samples from their employers at Cornell University, Harvard University, and UC Davis. Moreover, there have been numerous reports of Chinese biomedical researchers working at American universities, often on NIH grants, taking the IP their labs develop to China.<sup>353</sup> As the 2019 report of the U.S. China Economic and Security Review Commission to Congress concludes, IP theft has been a key reason for the emergence of China's biotech sector, which is becoming the world's leading producer of active pharmaceutical ingredients.<sup>354</sup>

## Domestic Preferences

Finally, some countries try to advantage domestic life-sciences producers through discriminatory procurement practices. China is one. For instance, the 2016 State Council Document on the industry stated, "In principle, government procurement projects must purchase domestically produced products and gradually improve the level of domestic equipment configuration of public medical institutions."<sup>355</sup> Some argue that China uses the drug import license as an industrial policy tool, limiting imports in order to give domestic firms a respite from foreign competition. For example, the government did not approve the 2015 renewal of Pfizer's license for the importation of its Prevnar 7 drug, a pneumococcal vaccine. Some have argued this was in order to give a domestic pneumococcal vaccine more time to be developed free from competition.<sup>356</sup> Likewise, Japan's Pharmaceutical PMP, the program responsible for ascertaining reimbursement levels the government pays for innovative medicines, includes preferences when companies conduct more clinical trials and launch new products early in Japan. And countries such as Brazil and Russia offer significant price preferences in government procurement for locally manufactured goods.<sup>357</sup>

## Acknowledgments

The author would like to thank Robert Atkinson, Joe Kennedy, Olivia Van Dervort, and Caleb Foote for their contributions to this report. Any errors or omissions are the author's alone.

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## About ITIF

The Information Technology and Innovation Foundation (ITIF) is a nonprofit, nonpartisan research and educational institute focusing on the intersection of technological innovation and public policy. Recognized as the world's leading science and technology think tank, ITIF's mission is to formulate and promote policy solutions that accelerate innovation and boost productivity to spur growth, opportunity, and progress.

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