

**RESPONSES TO QUESTIONS FOR THE RECORD**

**Regarding the Testimony of**

**Stephen J. Ezell**

**Vice President, Global Innovation Policy**

**Information Technology and Innovation Foundation**

**Before the**

**United States Senate**

**Committee on Finance**

**Hearing on**

**“Prescription Drug Price Inflation:**

**An Urgent Need to Lower Drug Prices in Medicare”**

March 16, 2022

Washington, DC

# QUESTIONS FOR THE RECORD FROM U.S. SENATOR MIKE CRAPO

## 1 a). On Problematic Claims regarding the House-passed Build Back Better Act

*A range of claims advanced in support of the drug price controls included in the House-passed Build Back Better Act (BBBA) warrant substantial scrutiny and skepticism.*

*Some backers of the bill have cited a January 2022 AARP piece suggesting that gas and milk prices would be astronomical if they had grown at the rate of prescription drug prices for the past fifteen years. Notably, however, the article in question relies on a June 2021 report using a dataset ending in December 2020, thus predating the recent surge in general inflation, which has coincided with far lower growth in drug prices. Moreover, the study in question focuses only on a subset of brand-name drugs, thus excluding the low-cost generics that account for 90 percent of the market, and its pricing metric fails to account for post-sale rebates and other price concessions. It also uses a fifteen-year window, which masks the recent slowing in even list price increases for medications.*

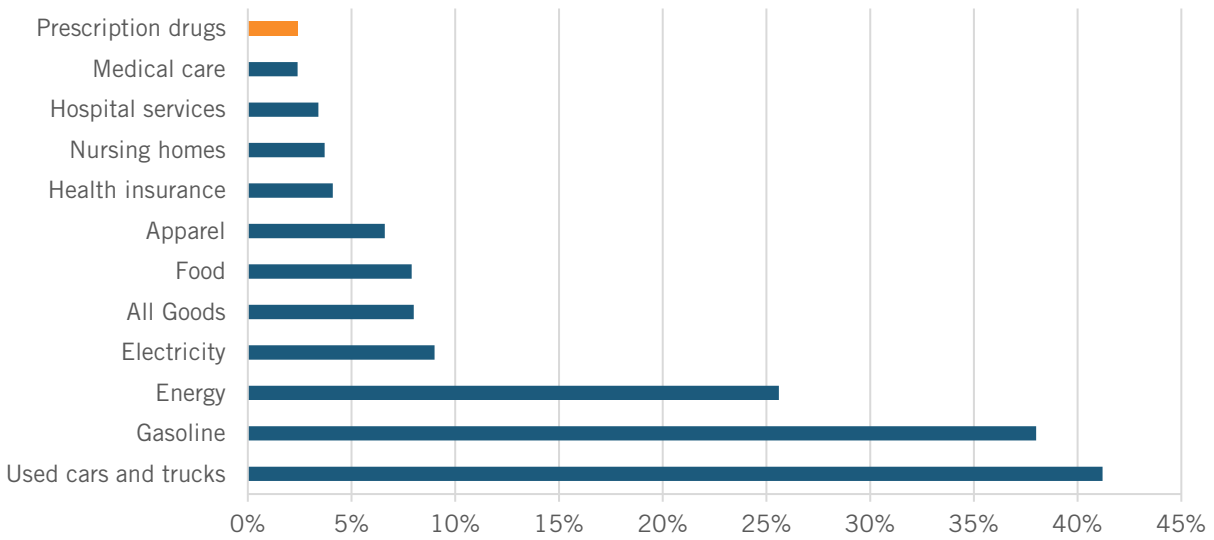
*In terms of the current wave of inflation eroding American families' finances, between February 2021 and 2022, general inflation (CPI-U) rose by 7.9 percent, while the consumer price index specific to milk increased by 11.2 percent and the gasoline-specific index surged by 38 percent. The prescription drug-specific index (CPI-Rx, which includes generics but still excludes post-sale rebates), by contrast, grew by just 2.4 percent.*

- *What metrics and studies provide the most accurate and inclusive data on price trends for prescription drugs?*
- *How does medication price inflation relate to general inflation and inflation specific to other goods cited by AARP, such as milk and gasoline?*

The best source for data on drug prices paid by U.S. consumers is actually the U.S. Bureau of Labor Statistics (BLS) and its Consumer Price Index (CPI). And this data shows that prescription drugs have in no way been a significant contributor to the increased inflation the United States is presently experiencing. In fact, over the past 12 months, prescription drug prices increased just 2.4 percent, well below the average CPI increase of 8 percent and less than other parts of the U.S. healthcare system, such as health insurance, which experienced a 4.1 percent increase. (See Figure 1.)

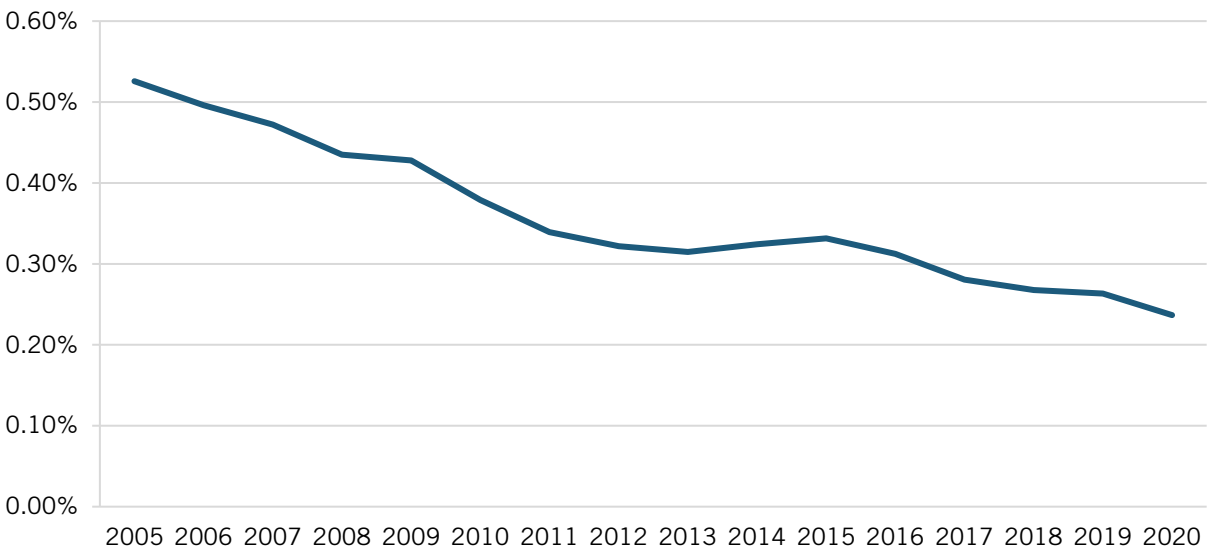
In fact, among the goods where U.S. consumers have faced dramatically increased inflation over the past year, drug prices didn't even make it within the top 100-highest price increases among the BLS itemized CPI (which tracks over 300 unique consumer expenditure categories). Moreover, between 2020 and 2021, BLS recorded zero inflation on prescription drugs and only a 0.8 percent price increase on non-prescription drugs. In the 12 months ending in February 2022, the cost of gasoline in the United States increased nearly 20 times more, 38 percent, than the cost of prescription drugs, 2.4 percent. Over that period, U.S. food prices increased by 8 percent, including a 6.9 increase for milk (for the 12-month period ending in January 2022).<sup>1</sup> Again, these price increases for food were considerably higher than the price increases for prescription drugs.

**Figure 1: Consumer price index by sector, 12-month change ending in February 2022<sup>2</sup>**



Moreover, Americans’ out-of-pocket drug expenditures, as a share of their personal income, have been considerably dropping over the past two decades. In fact, out-of-pocket drug costs are at an all-time low relative to total U.S. health spending. In 1960, out-of-pocket drug costs made up 9.5 percent of total U.S. health expenditures; today, that number is only 1.1 percent. In fact, consumers have consistently paid a lower share of their personal incomes toward out-of-pocket drug costs every year since 1960. The share of personal incomes in the United States paid toward out-of-pocket drug costs has halved over the last 15 years, from 0.53 percent in 2005 to 0.24 percent in 2020. (See Figure 2.)

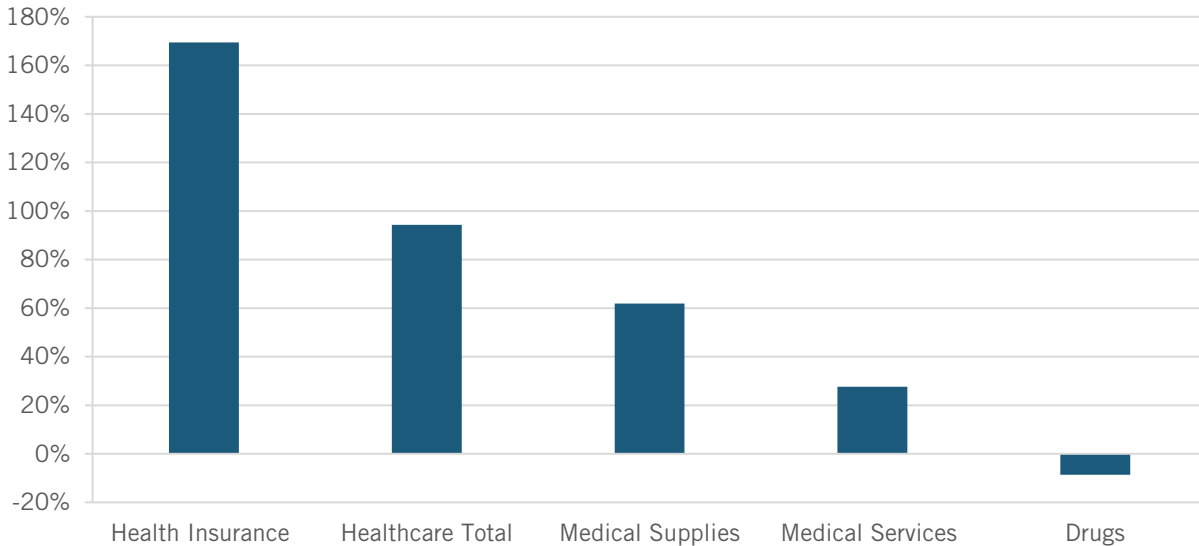
**Figure 2: U.S. out-of-pocket drug expenditures, as a share of personal income, 2005–2020<sup>3</sup>**



Indeed, as calculated by the U.S. Bureau of Labor Statistics, from 2005 to 2020, Americans’ reported expenditures on health insurance increased by over 160 percent, and total healthcare expenditures increased

94 percent, while consumer expenditures on drugs actually fell by almost 9 percent. (See Figure 3.) Of course, this does not necessarily mean overall drug expenditures fell because health insurance and hospitals also purchase drugs, but it does address consumers’ out-of-pocket costs. It’s reflective of a system that, broadly, both supports the creation of innovative drugs and then pathways for generic or biosimilar entrants to introduce price-decreasing competition.

**Figure 3: Percent change in consumers’ reported healthcare expenditures, 2005–2020<sup>4</sup>**



Another good source of data on U.S. healthcare expenditures is the Peterson-KFF Health System Tracker.<sup>5</sup> Data from Peterson-KFF show that the percentage of total U.S. health care spending going toward retail prescription drugs was consistent from 2000 to 2017, at mostly under 10 percent, and even dipped slightly to 8 percent in 2020.<sup>6</sup> Other good sources of data on health expenditure trends include Altarum’s report “Projections of the Non-Retail Prescription Drug Share of National Health Expenditures” and the report by Inmaculada Hernandez et al., “Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the US, 2007-2018.”<sup>7</sup>

*1b) In advocating for enactment of the BBBA’s drug pricing provisions, some have characterized the bill’s government price-setting program as market-based and fair, providing manufacturers with a say in the pricing of their products. These advocates have sought to differentiate the program from price controls and rate-setting mechanisms.*

*In reality, however, the legislation would allow the HHS Secretary to set any price of his or her choosing for virtually any product selected. Under the bill, noncompliance with any component of the price-setting program—including meeting bureaucratic deadlines, agreeing to participate in the program, and accepting the price that the federal government sets, however arbitrary or unrealistic—would trigger an unprecedented and seemingly unconstitutional noncompliance penalty of up to 95 percent of all gross sales across all markets. Manufacturers thus have no choice in the matter and no leverage in the process. The proposal would also permanently prohibit judicial and administrative*

*review of most elements of the new program, rendering any price set by the Secretary as absolutely final and enforceable.*

*In short, the bill provides for negotiation in name only.*

- *Is the government price-setting program created under the House-passed BBBA in any way negotiation? Does it, as its backers attest, rely on market forces and provide manufacturers with a meaningful say in setting prices?*
- *To your knowledge, has Congress enacted any provision resembling the 95 percent noncompliance penalty—nondeductible and applied across gross sales for all market segments—in modern political history?*

The BBBA does not establish a true “negotiation” of drug prices in Medicare; rather it’s more about arbitrary price setting that would enable the HHS secretary to dictate prices to manufacturers who would have little or no power to truly negotiate. As Doug Holtz-Eakin elaborates, “The BBBA would enshrine a unique and punitive 95 percent excise tax on gross profits on a therapy if the manufacturer does not agree to the secretary’s demands and set a ceiling for a drug’s price... Given the 95 percent excise tax the secretary would be free to wield against noncompliant innovators, ‘price extortion’ would be a more honest label for the provision than ‘price negotiation’.”<sup>8</sup> Moreover, unlike past proposals, there would be no floor price below which the secretary would be unable to force further concessions. As Holtz-Eakin continues:

While the BBBA would not apply Medicare’s negotiated prices for drugs to non-federal programs, the most significant implication of the BBBA’s dollar-for-dollar penalties on price increases that exceed the rate of inflation is that, for the first time, the federal government would be unilaterally capping drug prices nationwide, both in federal programs and in the private market. This shift in the federal government’s posture toward private markets, negotiations, and competition cannot be overstated. [Thus]... Significantly under the BBBA the federal government would cap the price of all drugs throughout the entire health care system by penalizing any manufacturer who increases a drug’s price faster than the rate of inflation.<sup>9</sup>

No, I am not aware of any instance in U.S. history where Congress has enacted any provision resembling a 95 percent non-compliance penalty. There is, however, considerable evidence of the damage that punitive excise taxes inflict on biomedical innovation. For instance, the Affordable Care Act imposed a 2.3 percent excise tax on the price of taxable medical devices sold in the United States from 2013 to 2015. A study by the Tax Foundation found that, even in the short time it was imposed, the tax resulted in higher prices as well as less research and development (R&D).<sup>10</sup> In fact, the Office of the Actuary for the Centers for Medicare and Medicaid Services stated that the medical device tax would ultimately increase national health care expenditures.<sup>11</sup> Moreover, the Tax Foundation found that if the medical excise tax had remained imposed as originally envisioned, it would likely have resulted in a decline of 21,390 full-time equivalent jobs and a reduction in GDP of \$1.7 billion.<sup>12</sup> But even in the mere three years in which the medical device tax was in place, it inflicted considerable damage on the U.S. medical device industry.<sup>13</sup>

The United States also has a broader history with government policies that attempt to set aggressive price controls, and their effect has generally been deleterious. For instance, in 1971, President Nixon’s Cost of

Living Council, led by Arnold Weber, attempted to quash inflation by temporarily blocking for 90 days increases in nearly all wages and prices. But it issued rules, such as one attempting to control prices in futures markets, that, in Weber's words, were "so contrary to established behavior that the markets simply shut down."<sup>14</sup> Nixon's price controls failed to stop inflation, reduced the value of the dollar by one-third, and were a significant contributor to the ensuing 1970s stagflation, as inflation persisted throughout the decade at an average annual rate of 8 percent.<sup>15</sup>

It's certainly true that some patients are paying more than they should for drugs at the pharmacy counter. Some reform is needed—notably to address the pinch seniors are experiencing in out-of-pocket costs at the pharmacy counter—but radical reconstructive surgery in the form of stringent drug price controls is not the solution.

*1c) BBBA's defenders sometimes argue that the life sciences sector is uniquely and exceptionally profitable and could thus easily absorb the costs triggered by the bill's price controls. Others argue that biopharmaceutical R&D estimates overstate the sector's commitment to innovative research, pointing to studies suggesting that marketing and advertising expenses for at least some segments of the industry exceed R&D investments.*

- ***Do these arguments accurately characterize the relative profitability, R&D intensity, and marketing/advertising expenditures of the biopharmaceutical sector? Why or why not?***

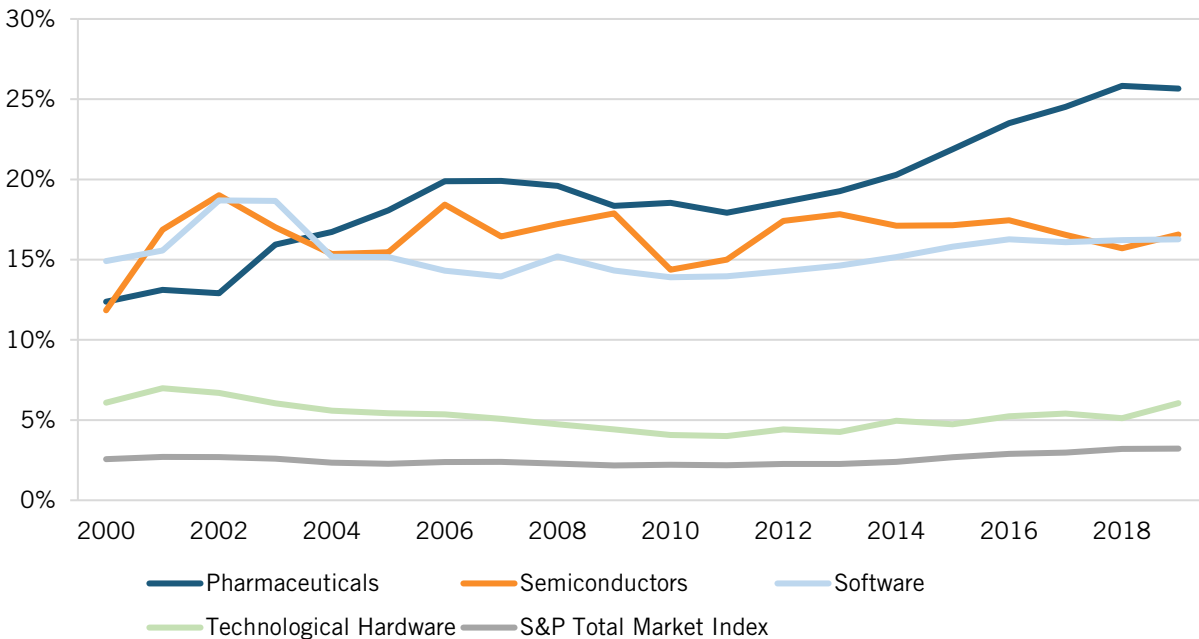
The U.S. biopharmaceutical industry is both America's and the world's most R&D-intensive industry—of any kind. As the U.S. Congressional Budget Office (CBO) explains, "Over the decade from 2005 to 2014, the industry's R&D intensity averaged 18 to 20 percent per year. That ratio has been trending upward since 2012, and it exceeded 25 percent in 2018 and 2019."<sup>16</sup> This level of R&D investment is substantially more than any other U.S. industry. As the CBO observes, "By comparison, average R&D intensity across all [U.S.] industries typically ranges between 2 and 3 percent" and even "R&D intensity in the software and semiconductor industries, which are generally comparable to the drug industry in their reliance on R&D, has remained below 18 percent."<sup>17</sup> (See Figure 4.) America's biopharmaceutical sector accounts for 18 percent of total U.S. business R&D investment.<sup>18</sup> Importantly, the CBO notes that while "Consumer spending on brand-name prescription drugs has risen, [the industry's] R&D has risen more quickly."<sup>19</sup>

The notion that America's innovative life-science industry is spending more on advertising than R&D is fundamentally specious. For that to be the case, the industry would have to be spending more than one-quarter of its total revenues on advertising, which it is not. According to the CBO, in 2019, the pharmaceutical industry invested \$83 billion dollars in R&D (which, adjusted for inflation, was an amount 10 times greater than the industry spent per year in the 1980s).<sup>20</sup> In contrast, total pharmaceutical advertising spending reached \$6.58 billion in 2020 (up modestly from the \$4.9 billion it was in 2007).<sup>21</sup>

Moreover this advertising isn't simply zero-sum, designed to gain market share over competitors. Rather, much of it is about educating consumers—and in the case of biopharma, educating healthcare providers, too—about choices.<sup>22</sup> Moreover, the drug industry is different than say the soap or car industry where it's relatively easy for consumers to find out on their own about new products and the differences between products. Some of the marketing expenses are to educate doctors and consumers about the value and efficacy of new drugs. This is why Frosch et al. find that more than half of physicians agree that ads educate patients

about health conditions and available treatments and nearly 75 percent of patient respondents agree that advertisements improve their understanding of diseases and treatments.<sup>23</sup>

**Figure 4: Average R&D intensity for publicly traded U.S. companies, by industry<sup>24</sup>**



The notion that the pharmaceutical industry is “exceptionally profitable” is also questionable. Researchers at the University of Southern California led by Professor Neeraj Sood have sought to estimate excess returns (the extent to which a firm’s profits are higher than expected given the risk associated with their investments) for manufacturers and middlemen in the pharmaceutical supply chain. They found that the rate of return on investments of large firms in the pharmaceutical industry between 2013 and 2018 was just 1.7 percent once adjusted for the risk premium paid for capital and the more logical treatment of R&D expenditures as long-term investments rather than current costs.<sup>25</sup> For comparison, the overall S&P 500 had an excess rate of return of more than double—3.6 percent—over this period.

The authors also found that other players in the pharmaceutical supply chain realized higher excess returns. Specifically, for the period from 2003 to 2018, they found that wholesalers earned excess returns of 8.1 percent and that insurers, pharmacy benefit managers (PBMs), and retailers collectively earned excess returns of 5.9 percent. The authors did find that the cohort of biotechnology firms in their study realized the highest excess returns of any group, at 9.6 percent, though they note this was in part driven by several blockbuster drugs introduced from 2013 to 2015, notably new Hepatitis C drugs, and that by 2018 the sector’s excess rate of return had fallen to under 9 percent. More importantly, however, the authors note that, “In contrast with middlemen, monopoly power in the pharmaceutical and biotech sectors—derived through the U.S. patent system—provides [an] incentive for innovation that might not happen otherwise.”<sup>26</sup>

But the point here should be the value these industries are delivering for society relative to their degree of profitability. America’s life-sciences innovators are delivering innovative drugs that have accounted for 73 percent of the increase between 2000 and 2009 in life expectancy at birth across 30 countries, including the

United States (or 1.27 years of the 1.73-year increase in life expectancy).<sup>27</sup> Moreover, America's life-sciences companies employ approximately one-quarter of America's total R&D workforce. Meanwhile, 23 percent of the American biopharmaceutical industry's workforce can be found at the lab bench in R&D jobs seeking to create new cures, giving the industry a share of employment dedicated to R&D three times higher than the national average.<sup>28</sup> Those numbers represent tremendous returns and value to society, especially relative to profitability; PBMs, according to Sood's data, are more profitable than pharmaceutical firms and almost as much so as biotechnology ones, but they're not nearly employing one-quarter of America's R&D workforce or developing products that have tremendous impacts on American and global citizens' quality and length of life.

Lastly, many BBBA proponents assert that America's life-sciences innovators aren't focused on breakthrough innovation or just focus on "me-too" drugs. But the reality is that there are currently 4,500 medicines under development in the United States, including 560 seeking to treat pediatric diseases, 537 for neurological diseases, 362 for cell and gene therapies, and hundreds more for mental illness, asthma and allergies, and other maladies.<sup>29</sup> Many of these are potentially "first-in-class" drugs, including 86 percent for Alzheimer's, 79 percent for various forms of cancer, 75 percent for psychiatry, 74 percent for neurology, and 73 percent for cardiovascular disease.<sup>30</sup> To assert that the industry, broadly, isn't working to develop breakthrough treatments is fundamentally fallacious.

And trying to make progress in many of these fields is extremely difficult. For instance, consider that between 1998 and 2017, there were 146 attempts to bring new Alzheimer's treatments to market, but just 4 out of those 146 were successful approvals. In other words, 97 percent proved unsuccessful.<sup>31</sup> (However, the value of a successful treatment would be profound: the United States could save \$220 billion within the first five years and a projected \$367 billion in the year 2050 alone if a cure or effective treatment for Alzheimer's disease could be found.)<sup>32</sup>

The difficulty of innovating safe and effective new drugs is further illustrated both by efforts to develop oncology drugs and to develop vaccines in response to the COVID-19 pandemic. A 2019 study by Wong, Siah, and Lo examining oncology drug development efforts from January 1, 2000 to October 31, 2015 found that oncology programs have just a 3.4 percent chance of ultimate Food and Drug Administration (FDA) approval (and yet companies continue to invest tens of billions of dollars trying to tackle oncology challenges).<sup>33</sup> Similarly, life-sciences companies responded with great alacrity in attempting to develop COVID-19 vaccines and therapeutics. But thus far, only 2 of 58 vaccine attempts (3.4 percent) have received final approval (18 are in Phase III clinical trials). But already 26 vaccine candidates have failed, as well as 54 proposed antiviral medications and 90 different therapeutic treatments.<sup>34</sup>

*d) In making the case for the House-passed BBBA drug pricing policies, some have suggested that most new drugs that come to market are 'me-too' products that either make modest changes to existing medications or treat conditions that already have numerous therapeutic options. These claims seem at odds with the drug development landscape, where the majority of the 50 new drugs approved last year were first-in-class treatments, and where studies regarding existing therapies can lead to new indications and uses, along with improvements that offer outsize patient benefits. One drug originally indicated to treat chronic lymphocytic leukemia, for instance, received approval as a disease-modifying therapy (DMT) for the treatment of multiple sclerosis roughly eleven years later, after a far-*



reaching and costly clinical development program. This type of follow-on innovation can result in major medical breakthroughs.

- *To what extent do we see meaningfully innovative drugs and biologics approved each year, and what potential value does follow-on innovation offer to patients?*
- *How would the government price-setting program and other price controls included in BBBA impact incentives for follow-in innovations like new indications for existing therapies, new formulations (i.e. to mitigate or eliminate side effects, to streamline dosing regimens, etc.), and other product improvements and changes?*
- *While the House-passed BBBA technically makes no changes to patents and exclusivities with respect to prescription drugs, the government price-setting program and multi-market price growth cap policies would affect a manufacturer's ability to derive economic value from these market protections. How would the bill's price controls impact the incentives for innovation currently inherent in patents and exclusivities?*

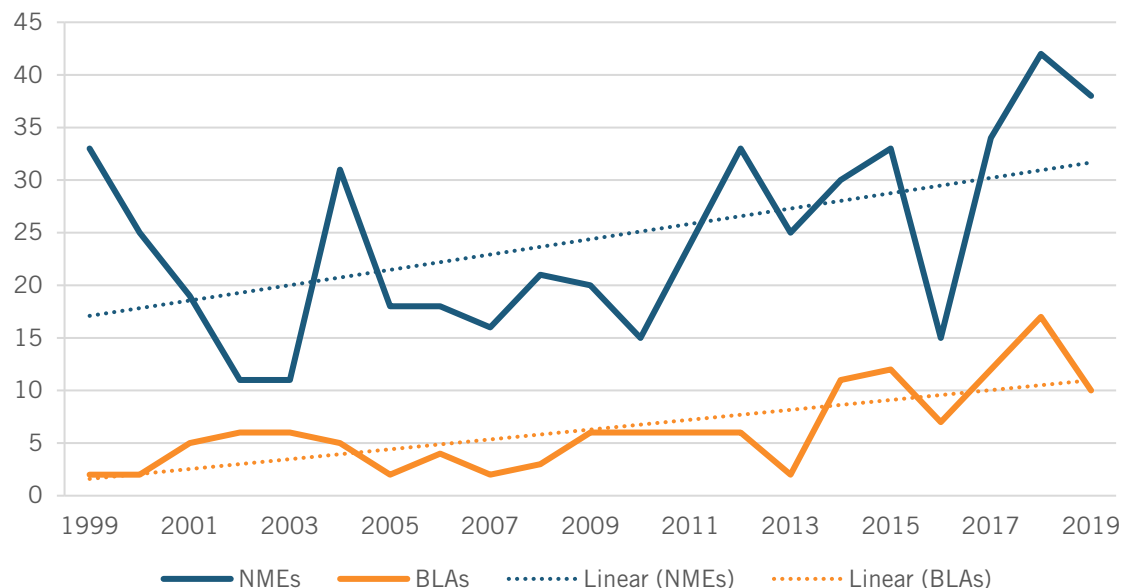
As just noted, contrary to critics' assertions, America's biopharmaceutical industry is an innovation-oriented one, not a me-too-oriented one.

In 2020, the FDA's Center for Drug Evaluation and Research (CDER) approved 53 novel drugs.<sup>35</sup> Of these novel drugs, 21 were considered first-in-class and 31 were designated orphan drug status.<sup>36</sup> Similarly, the FDA's Center for Biologics Evaluation and Research (CBER) approved eight biologics.<sup>37</sup> The year 2020 also saw the first therapeutics for COVID-19 and some forms of premature aging, such as progeria.<sup>38</sup>

Similarly, in 2021, CDER approved 50 novel drugs, and CBER approved 10 new biologics.<sup>39</sup> Despite the slight overall decrease in novel drugs, 27 were given first-in-class designation, and 26 were granted orphan drug status.<sup>40</sup> Although it is too early in 2022 to provide significant data, the FDA lists 10 novel drugs and 2 biologics already approved as of April 21, 2022, along with 9 new generics or biosimilars.<sup>41</sup>

And despite critics' assertions the reality is that new drug approvals have significantly accelerated over the past two decades. The FDA's Center for Drug Evaluation and Research's five-year rolling approval average stood at 44 new drugs per year in 2019, double the lowest five-year rolling average of 22 drugs approved, realized in 2009. (See Figure 5.) And the number of drugs in development globally increased from 5,995 in 2001 to 13,718 in 2016.<sup>42</sup>

**Figure 5: FDA annual approvals of new molecular entities (NMEs) and biologics license applications (BLAs), 1999–2019<sup>43</sup>**



Yet, as Representative Katie Porter (D-CA) argues in her report, “Killer Profits: How Big Pharma Takeovers Destroy Innovation and Harm Patients,” “Instead of taking risks to find new, critically needed drugs, large pharmaceutical companies are just repackaging the same products over and over: In 2018, only 1 in 3 new brand-name drugs that drug companies launched were ‘first-in-class’ drugs.”<sup>44</sup> Similarly, Rena Conti observed in her Senate Finance Committee hearing testimony that “Sanofi testified in the Senate that only 33 of its 81 R&D projects were for new chemical entities” (again, about one-third).<sup>45</sup>

Is 1 in 3 low? In the 1940s and 1950s, when there were few drugs on the market and almost all were first in class, 1 in 3 would have been low. But as more drugs hit the market, the share of first-in-class drugs declined as it became harder to discover new treatments and also because of the importance of producing multiple drugs to address the same disease. Nonetheless, the share of drugs that are new has risen since the 1970s, not fallen.<sup>46</sup>

Moreover, criticisms of the industry for when it does invest in “me-too” drugs fails to recognize the significant clinical benefits of new drugs complementing existing drugs. Sometimes an existing drug does not perform as well as the new drug. Sometimes certain individuals have adverse reactions to an existing drug but not the new drug.<sup>47</sup> In addition, follow-on drugs can be better in efficacy or methodology and convenience of use and administration. DiMasi and Faden found that 32 percent of follow-on drugs have received a priority rating from the U.S. FDA, indicating that these drugs are likely to provide an important improvement over the first-to-market drug.<sup>48</sup> They concluded, “Overall, these results indicate that new drug development is better characterized as a race to market among drugs in a new therapeutic class, rather than a lower risk imitation of a proven breakthrough.”<sup>49</sup> Moreover, the Government Accountability Office (GAO) found that the introduction of additional drugs lowers prices.<sup>50</sup>

Indeed, follow-on innovations from original innovative drugs represent an important aspect of America’s life-sciences innovation system that can bring important benefits for patients. These can include new indications (i.e., applications of an existing drug to a new disease), improvements in delivery forms (i.e., providing a

medication orally as opposed to through an injection), or improvements in delivery dosages (i.e., a pill administered once a month as opposed to once daily).

For instance, in 2013, a revolutionary new treatment called Solvadi was released that boosted Hepatitis C cure rates to 90 percent. This was followed in 2014 by an improved treatment called Harvoni, which cures the Hepatitis C variant left untouched by Solvadi. By early 2020, an astonishing six new treatments for the disease had received FDA approval, opening up a wide range of treatment options that take into account patients' liver and kidney status, co-infections, potential drug interactions, previous treatment failures, and the genotype of the HCV virus.<sup>51</sup> Moreover, as competitors joined the market, the price of Sovaldi was cut in half.<sup>52</sup>

The provisions in the BBBA would likely have a deleterious impact on both follow-on and generic drug innovation. That's in no insignificant part because generic or biosimilar drugs depend, by definition, on the innovative drugs or biologics that predated them, and when drug price controls inhibit the creation of innovative medicines in the first place, they tamp down on the capacity to create the cheaper generics or biologics of tomorrow, a dynamic that would only be amplified by artificially decreasing the price of innovative drugs through price controls. As Holtz-Eakin elaborates:

Ironically, the more successful the HHS secretary is in leveraging the BBBA's punitive excise tax to force price concessions, the fewer generic and biosimilar products are likely to come to market. Follow-on products are able to dramatically undercut name-brand drugs and biologics on price because they do not have the same R&D expenditures and because their lower prices allow them to achieve larger market shares. But if the price difference between a name-brand drug, subject to the secretary's price controls, and a new generic is marginal or even non-existent, the ability of a generic to gain market share will be reduced.<sup>53</sup>

As to the long-term effect of the BBBA on the subsequent number of generic drugs, the University of Chicago's Tomas Philipson and Troy Durie reach a similar conclusion, writing:

We looked at the patent life and data exclusivity of the top 20 drugs by total Medicare Part B and D spending, finding that this plan will shorten their market life by 2-4 years on average. These drugs will no longer have the advantages of exclusivity by having an artificially lower price, but cheaper generics still will not be able to be developed while they watch the government price them out of the market. This new price control scheme will lead to fewer generics and less competition which has been shown to lead to effective price reductions without undermining innovation.<sup>54</sup>

*e) Some have claimed that the BBBA's drug pricing provisions would exempt startups and other small biotechs from the onerous new government price-setting program included in the legislation. In reality, however, the bill includes only an extremely narrow and time-limited exemption that carves certain small biotechs out of the program for three years and provides them with a pricing floor for the following two, after which point the bureaucratic new system would treat these small firms like any other companies. Notably, 66 percent of biopharmaceutical companies are startups. Moreover, small businesses—many of which would not qualify for even the temporary exemption—account for 70 percent of pivotal-stage trials, and more than 90 percent of biopharmaceutical firms overall are not turning a profit.*

- *Do the time-limited and narrow small biotech exemptions in the bill provide meaningful protection for the startups and other small businesses that comprise the majority of the life sciences sector?*
- *If enacted, how would the government price-setting program and other price controls (such as the mandatory multi-market price growth cap) impact these small businesses and the prospects of future biopharmaceutical startups?*
- *How might the imposition of the bill's price controls fuel industry consolidation, given the diversified product portfolios and compliance-related resources and staff that large multinationals often enjoy, relative to smaller businesses?*

Proponents assert that life-sciences could easily absorb the costs of the BBBA drug price controls. But, while that might be easier, though still deleterious, for larger firms, it forgets that start-ups account for 66 percent of U.S. biopharmaceutical enterprises.<sup>55</sup> Yet these startups, 90 percent of which are pre-revenue, account for 70 percent of drugs in phase III clinical trials.<sup>56</sup> Yet government price controls, even if there is some type of carve out for small innovators, would still sharply reduce the opportunity to earn a return. One reason is that acquisition by a larger company often represents an important, and legitimate and meritorious, exit strategy for a smaller company and to the extent the BBBA deprives larger firms of revenues, this would reverberate throughout the ecosystem. But, overall, such drug price controls would harm small and large biopharmaceutical firms alike.

*f) Therapeutic development relies heavily on high-risk investments from diverse sources. While some of the BBBA's backers anticipate that the life sciences would remain attractive to investors at every level, real-world experience tells a different story. Even under current laws and regulations, capital can—and often does—shift away from (or simply never flow into) the biopharmaceutical sector. According to one WSJ piece from last December, for instance, biotech stocks “crumbled” in 2021.*

*Developing a new medication can take between 11.5 and 15 years, and only one in every 1,000 drug formulas ever enters preclinical trials. For the ones that do, only eight percent ever receive FDA approval. Unsurprisingly, it costs an average of \$2.6 billion to develop and gain approval for a new medicine. These factors make the biopharmaceutical sector especially sensitive to the types of government price controls included in the House-passed BBBA, which University of Chicago researchers projected would lead to 135 fewer new drug approvals in the next two decades.*

- *How would the price controls included in the BBBA likely impact the investment landscape with respect to biopharmaceutical innovation?*

*g) Supporters of the BBBA's government price-setting program sometimes cite the Veterans Affairs (VA) Department as a model for Part D. In practice, however, the closed formulary leveraged by the VA impairs access to many medications. Among the top 200 Part D drugs by overall spend, for instance, one study found that Part D plans covered an average of nearly three-fourths of the products, while the VA covered just over half. Among a sample of 25 first-in-class treatments, Part D plans covered more than three in every five, while the VA covered just 40 percent. The VA also integrates value assessments using quality-adjusted life years (QALYs) into its pricing practices,*

*despite widespread criticism of these metrics by disability advocates, who argue that QALYs devalue individuals with exceptional needs, along with older individuals.*

Life-sciences companies depend on profits from one generation of biomedical innovation to fund investment in the next. Research by Dubois et al. makes this dynamic crystal clear, finding that every \$2.5 billion of additional biopharmaceutical revenue leads to one new drug approval.<sup>57</sup> Related 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>58</sup> Likewise, Gambardella found that sales revenue from previous periods have a significant, positive impact on current-period biopharma R&D.<sup>59</sup> Henderson and Cockburn find that the pharmaceutical firms with the greatest sales are also the ones with the largest R&D investments.<sup>60</sup> Drug price controls would harm future investments in biomedical innovation.

- *Is the VA drug pricing system an appropriate model or exemplar for Part D? Why or why not?*

The VA approach doesn't provide a satisfactory exemplar for Medicare Part D, that's especially because, unlike Medicare Part D, the VA employs a "one-size-fits all" approach that limits access to medicines. It's a closed formulary. In particular, "the VA employs a narrow, exclusionary formulary to generate savings, and comparisons of coverage between the VA and Medicare demonstrate that the VA offers fewer choices, particularly of the most cutting-edge and innovative medicines."<sup>61</sup> For instance, considering the top-200 Part D brand medicines, a July 2020 study found that, while 74 percent were covered by Medicare, just 52 percent were covered by the VA formulary. Likewise, the VA National Formulary covers just 40 percent of first-in-class Part D medicines, compared with more than 62 percent in Medicare Part D.<sup>62</sup> As the GAO explains, while "the VA can steer utilization toward a limited number of drugs within a given therapeutic class; Medicare Part D plans, on the other hand, generally have broad networks of pharmacies and as such may have broader formularies than VA's."<sup>63</sup> Moreover, because of limitations on the VA formulary, to acquire access to the medicines they need, more than half of all veterans supplement their VA benefits with other sources of health coverage, including Part D.<sup>64</sup> The VA's use of QALYs also discriminate against the disabled, seniors, the chronically ill and communities of color; for instance, a QALY for a patient with multiple sclerosis can be worth half as much as a healthy, young individual, and a person over the age of 70 is worth approximately 30 percent, simply due to their age.

*h) In defending the government price-setting program and multi-market price growth cap policies in the BBBA, some policymakers have contended that under current law, manufacturers enjoy maximal price-setting power and can charge whatever they want, while purchasers and consumers lack any leverage. In practice, however, all three of the largest pharmacy benefit managers (PBMs) exclude between 400 and 500 drugs from their standard formularies, and the number of drugs excluded by these formularies increased by 676 percent from 2014 to 2020. Moreover, rebates paid by manufacturers have grown substantially in recent years, further reducing net prices and demonstrating leverage on the part of the payers extracting these price concessions.*

- *Do drug manufacturers, as many BBBA supporters argue, enjoy absolute power to charge whatever they want?*

No, drug companies do not enjoy absolute power to charge whatever they want. Drug companies face many constraints: on the innovation side they're constrained by science, which is why, 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>65</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>66</sup> It's why oncology drug efforts have only a 3.4 percent chance of winning FDA approval.

When drugs do make it to market, even the ones getting there first will often quickly face competition. For instance, as noted previously, as competitors joined the market, the price of Sovaldi as not just a treatment but an actual cure for Hepatitis C was cut in half. Further, innovative drugs have a limited period of patent protection, and when drugs go off patent, much cheaper generic drugs often come rapidly on the scene. As noted subsequently in response to a question from Senator Sasse, for instance, once Biogen's multiple sclerosis (MS) drug Tecfidera went off-patent, generic competitors entered with drugs well over 95 percent cheaper. Lastly, of course, drug makers must negotiate with pharmacy benefit managers and other wholesalers to get their drugs listed on formularies like Medicare Part D, where the negotiations are aggressive. Some argue that there's no negotiation function for Medicare Part D, and thus the government needs to take the process over. But the issue isn't negotiation or no negotiation. There is negotiation, for instance as provided by the PBMs; policymakers should focus on helping this market-based process function better, such as through increasing scrutiny and transparency on PBMs and ensuring they meet their fiduciary obligations.

### ***3. On List Price Growth***

*While net prices for brand-name drugs have fallen for at least four consecutive years, according to IQVIA and others, list prices for these products have grown—albeit at a slower rate than in previous years.*

- ***What are some of the underlying factors driving list price growth for prescription drugs?***

When it comes to the growing disparity between drugs' list and net prices, particular attention must be paid to the role played by rebates and discounts. Discussion of drug prices tends to focus on the annually announced increase in the list prices for prescription drugs. However, sales of prescription drugs are subject to substantial manufacturer rebates and discounts, leading to a considerable reduction in manufacturer earnings. Researchers at the University of Pittsburgh School of Pharmacy and Medicine estimate that while the average annual increase in the list price for prescription drugs between 2007 and 2018 was 9.1 percent, the net increase in drug prices after rebates was only 4.5 percent.<sup>67</sup>

In recent years, as list prices have been growing at a slower pace, the volume of discounts and rebates has increased. For example, in 2020, list prices grew at an average rate of 4.4 percent, but net prices decreased by 2.9 percent.<sup>68</sup> As the *Wall Street Journal*, citing data from the SSR Health Report, notes, “[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>69</sup> (See Figure 6.)

**Figure 6: Change from a year earlier in U.S. prescription brand prices, 2009–2019<sup>70</sup>**



In fact, one study found that more than one-third of drug list prices were rebated back to PBMs and other entities in the supply chain. 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>71</sup>

Fees charged by intermediaries also subtract from drug manufacturer revenues. PBMs nearly quadrupled the fees they charge biopharmaceutical companies—such as administrative and service fees—between 2014 and 2016. Total fees charged to biopharmaceutical companies by these middlemen increased from \$1.5 billion in 2014 to \$2.6 billion in 2015, and then doubled to nearly \$5.6 billion in 2016. Along with rebates, these fees—which are typically based on the list price of a medicine—contribute to a system of misaligned incentives where middlemen make more money when the list prices of medicines increase.<sup>72</sup>

Despite an increase in the share of negotiated rebates shared with health plan and employer clients, total PBM revenue increased considerably between 2014 and 2016. That’s in part due to the increasing administrative fees they charged biopharmaceutical companies. But PBMs aren’t just charging biopharmaceutical companies more than ever before—they also brought in a record total of \$22.4 billion in revenue in 2016 by charging more to others in the supply chain, such as health plans and pharmacies.<sup>73</sup>

For further input on the factors driving list price growth in medicines, please see the response to Senator Sasse’s question on insulin pricing which follows subsequently.

#### **4. On Public Funding and Innovation**

*NIH and its grantees unquestionably conduct crucial foundational research. Through scores of strategic public-private partnerships, our current system enables research institutions and job creators of all sizes to translate and transform NIH-supported basic research into tangible biomedical breakthroughs, from diagnostic tests to treatments and cures.*

*That being said, proposals to replace private R&D-driven capital with taxpayer dollars raise serious concerns. Public and private research support should play complementary roles—not conflicting ones—and the federal bureaucracy is no substitute for private-sector innovation and expertise.*

*According to one study, in fact, when it comes to life sciences research resulting in a new medical innovation, the private sector invests as much as \$100 in development for every \$1 invested by the government. Along those lines, a survey of some of the most transformational medicines to reach the market in recent years found that whereas public funding played a critical role in achieving basic science milestones, private industry led the way for milestones related to drug discovery, production, and development, often by staggering margins.*

- ***Do you see public funding as an adequate substitute for any private-sector shortfalls that might result from government-mandated price controls?***

The complementarity between the respective U.S. public and private sectors to biomedical innovation has been one of the great strengths of the U.S. approach to biomedical innovation. Public funding for basic life-sciences research, especially through the National Institutes of Health (NIH), funds basic discoveries such as into understanding the fundamental processes by which diseases develop and are transmitted or identifying novel biomarkers that signal the presence of a disease. This creates a body of knowledge which represents a platform for innovation by the private sector to try to turn novel molecules into safe drugs. Private-sector activity centers on applied R&D focused on the discovery, synthesis, testing, and manufacturing of candidate compounds intended to exploit biologic targets for the purpose of curing medical conditions. As Chakravarthy et al., note, “Without private investment in the applied sciences there would be no return on public investment in basic science.”<sup>74</sup> Indeed, it’s critical to remember that considerable investment is required to bring a drug to market even after considerable amounts of basic research have been conducted. In fact, one study by Chatterjee and Rohrbaugh found that biotechnology companies invest \$100 in development for every \$1 the government invests in research that leads to an innovation.<sup>75</sup>

Public funding would simply not be an adequate substitute for private-sector shortfalls that might result from government-mandated that price controls. That notion is as misguided as other proposals which would call for the government to take over the principal role of drug development from the private sector. Nevertheless, in their quest to shrink the for-profit drug discovery and development industry, drug populist advocates have floated a variety of such proposals, such as: having employers pay a medical research fee, which they would allocate to any research organization, including government; subjecting firms to compulsory licenses (where they must make patented discoveries available to other firms) but having the government pay patent holders directly to compensate them; having the government buy patents from firms through an auction; establishing government-funded corporations to develop and sell drugs; using prizes; and, finally, giving NIH the task.



For example, Dean Baker of the Center for Economic Policy Research writes, “We could expand the public funding going to NIH or other public institutions and extend their charge beyond basic research to include developing and testing drugs and medical equipment.”<sup>76</sup> Knowledge Ecology International, a leading drug populist organization, has advocated eliminating drug patents and instead having the government issue prizes for drug development. It cites proposed legislation by Senator Bernie Sanders (D-VT) to create a Medical Innovation Prize Fund that would equal 0.55 percent of U.S. GDP, an amount greater than \$80 billion per year, with the federal government funding half and private health insurance companies the other half.<sup>77</sup>

But as the Information Technology and Innovation Foundation (ITIF) writes in “Delinkage Debunked: Why Replacing Patents With Prizes for Drug Development Won’t Work,” separating the cost of biopharmaceutical research and development from the final market price of medicines would misalign incentives, raise bureaucratic costs, and limit innovation.<sup>78</sup> Indeed, while advocates claim that “delinking” drug prices from R&D investments would make innovative medicines far cheaper, the truth is it would almost surely lead to less new drug development and slower progress in improving human health.

For instance, for prizes to work globally, governments would have to replace at least \$200 billion per year in private medical R&D with taxpayer funds, which is unlikely given the budget challenges many governments face and the fact many of the benefits would flow to other countries.<sup>79</sup> Consider that as part of the World Health Organization’s (WHO) push to increase investment in global health R&D, WHO member states in 2013 agreed to establish a Global Observatory on R&D to monitor spending and set priorities, and also to undertake a number of global health R&D demonstration projects. At the World Health Assembly in Geneva in May 2017, Marie-Paule Kieny, WHO assistant director-general for Health Systems and Innovation, remarked on the chronic underfunding of this “critically important” agenda, noting that one of the demonstration projects (on a nano-based malaria drug delivery system) is being cancelled unfinished due to a lack of funding.<sup>80</sup>

According to the WHO, \$85 million was needed between 2014 and 2017 to complete these projects, yet by the end of 2016, only \$11 million had been committed by only 10 WHO member states, leaving a shortfall of \$73 million.<sup>81</sup> WHO’s website on the R&D demonstration projects has not had any significant updates in several years.<sup>82</sup> A \$73 million shortfall is one thing; a roughly \$200 billion shortfall would be another. Put simply, if WHO members cannot agree among themselves to provide the relatively small amounts of funding for even this modest agenda, it seems highly unlikely they would stump up the hundreds of billions of dollars required to implement advocates’ delinkage proposals.

Moreover, the true value of a new medicine is hard to measure before it is created, so prizes could be underfunded. That would lead to fewer companies taking the risk of investing in expensive R&D, and hence to fewer new medicines. Lastly, handing over significant control of national or global biomedical R&D flows to government bodies represent a recipe for inefficiency and for politicizing drug development. The current market-based system of drug development allows for experimentation and competition within and between therapeutic classes. Thousands of promising leads enter the drug development pathway, but only a few make it through the rigorous process of clinical trials. The cost of failures and the risks are borne almost entirely by the private sector at no cost to taxpayers. As Daniel Spulber, Professor of International Business at the Kellogg School of Management, Northwestern University, and an award-winning expert on innovation policy, concludes, “There is nothing wrong with awarding prizes. But replacing markets for medicines with

government prizes would destroy one of the most innovative areas in the economy, and stop the endless source of life-saving medicines.”<sup>83</sup>

## **5. On Public-Private Partnerships and Innovation**

*Mr. Ezell, you have written extensively on the importance of public-private partnerships in advancing and ensuring access to innovation, as enabled by the bipartisan Bayh-Dole Act. Some advocates and policymakers have proposed a radical reinterpretation of this framework, arguing that the federal government should “march in” to seize or forcibly license patents to cut costs.*

*Both of the Bayh-Dole Act’s sponsors spent decades emphatically opposing this revisionist rewriting of so-called march-in rights, which could prove particularly harmful for patients with unmet medical needs, as well as research institutions and small businesses across all of our states.*

- ***What was the original intent behind the march-in provisions in question, and how would this sweeping reinterpretation impact public-private partnerships and American innovation more broadly?***
- ***How does the current ecosystem benefit universities and nonprofit research institutions, and how might the aggressive use of march-in rights impact their financial standing, particularly with respect to royalty income?***

The 1980 Bayh-Dole Act permits universities to patent their researchers’ inventions, even if that research was partly funded by the federal government. The Act has played a pivotal role in catalyzing U.S. life-sciences innovation and creating a pathway to realize value creation from federally funded research.<sup>84</sup> Consider that at the end of the 1970s, the U.S. government had licensed fewer than 5 percent of its 28,000 patents, but the number of patents from government-funded research shot up over tenfold in the years since Bayh-Dole, reaching more than 40,000 in 2017.<sup>85</sup> And since its introduction, Bayh-Dole has enabled more than 15,000 startups launched from U.S. universities as well as 300 new medicines based on patented discoveries.<sup>86</sup>

The Bayh-Dole Act includes so-called “march-in rights” that permit the U.S. government, in very limited and specified circumstances, to require patent holders to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.”<sup>87</sup> The four circumstance in which the government is permitted to exercise march-in rights are:

1. If the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention;
2. If action is necessary to alleviate health or safety needs not reasonably satisfied by the patent holder or its licensees;
3. If action is necessary to meet requirements for public use specified by federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
4. If action is necessary, in exigent cases, because the patented product cannot be manufactured substantially in the United States.<sup>88</sup>

In other words, lower prices are not one of the rationales laid out in the Bayh-Dole Act as a valid justification for the use of march-in rights. In fact, as senators Bayh and Dole have themselves noted, the Bayh-Dole Act's march-in rights were never intended to control or ensure "reasonable prices."<sup>89</sup> As the twain wrote in a 2002 *Washington Post* op-ed titled, "Our Law Helps Patients Get New Drugs Sooner," the Bayh-Dole Act:

Did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. This omission was intentional; the primary purpose of the act was to entice the private sector to seek public-private research collaboration rather than focusing on its own proprietary research.<sup>90</sup>

The op-ed reiterated that the price of a product or service was not a legitimate basis for the government to use march-in rights, noting:

The ability of the government to revoke a license granted under the act is not contingent on the pricing of a resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product.<sup>91</sup>

Rather, the Bayh-Dole Act's march-in provision was designed as a fail-safe for limited instances in which a licensee might not be making good-faith efforts to bring an invention to market, or when national emergencies require that more product is needed than a licensee is capable of producing. This is why the National Institute of Standards and Technology (NIST) report "Return on Investment Initiative: Draft Green Paper" agrees, noting, "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>92</sup> The report notes that, "NIH determined that that use of march-in to control drug prices was not within the scope and intent of the authority."<sup>93</sup> Indeed, march-in rights have never been exercised during the now-42-year history of the Bayh-Dole Act.<sup>94</sup>

The argument that Bayh-Dole march-in rights could be used to control drug prices was originally advanced in an article by Peter S. Arno and Michael H. Davis.<sup>95</sup> They contended that "[t]he requirement for 'practical application' seems clear to authorize the federal government to review the prices of drugs developed with public funding under Bayh-Dole terms and to mandate march-in when prices exceed a reasonable level" and suggested that under Bayh-Dole, the contractor may have the burden of showing that it charged a reasonable price.<sup>96</sup> While Arno and Davis admitted there was no clear legislative history on the meaning of the phrase "available to the public on reasonable terms," they still concluded that, "[t]here was never any doubt that this meant the control of profits, prices, and competitive conditions."<sup>97</sup>

But as John Rabitschek and Norman Latker explain, there are several problems with this analysis. First, the notion that "reasonable terms" of licensing means "reasonable prices" arose in unrelated testimony during the Bayh-Dole hearings. Most importantly, they note, "If Congress meant to add a reasonable pricing requirement, it would have explicitly set one forth in the law, or at least described it in the accompanying reports."<sup>98</sup> As Rabitschek and Latker continue, "There was no discussion of the shift from the 'practical application' language in the Presidential Memoranda and benefits being reasonably available to the public, to benefits being available on reasonable terms under 35 U.S.C. § 203."<sup>99</sup> As they conclude, "The interpretation

taken by Arno and Davis is inconsistent with the intent of Bayh-Dole, especially since the Act was intended to promote the utilization of federally funded inventions and to minimize the costs of administering the technology transfer policies.... [The Bayh-Dole Act] neither provides for, nor mentions, ‘unreasonable prices.’”<sup>100</sup>

Simply put, the Bayh-Dole Act does not give the U.S. government the right to march-in on the intellectual property (IP) of a company that has developed a product in whole or in part based on discoveries that may have originated in whole or in part from federally funded research simply because the government does not like the price of the resulting product. The reality is that (mis)using march-in rights or establishing new ones in order to control drug prices would result in fewer new drugs. Companies would be highly reticent to spend billions developing a drug if they knew the government could come in as long as two decades later and seize or compulsorily license their IP in order to control drug prices.

If the government began to use march-in rights on a regular basis to control drug prices, or the prices of other innovations, such as in the information technology (IT) or clean energy sectors, it would almost certainly have a deleterious impact on U.S. universities and their ability to earn royalties as a result of academic technology transfer activities. That matters when today many universities list technology commercialization as one of their top-five strategic priorities and university presidents often mention technology transfer as a key differentiator for their universities.<sup>101</sup> In 2018, U.S. universities directly generated approximately \$2.94 billion in licensing revenue from the process of taking academic inventions to market. The Bayh-Dole Act has played a critical catalytic role in turning America universities into engines of innovation, a dynamic that would certainly be undermined if the government started to actively (mis)use Bayh-Dole march-in rights to attempt to control the prices of drugs or other products.

## **6. On Global Leadership and Competition**

*The United States has emerged, in recent decades, as the global leader on life sciences innovation, with the world’s most cutting-edge R&D, spearheaded largely by our research universities and by small businesses. Government price controls and top-down mandates, however, risk jeopardizing our position and enabling our global rivals—particularly China—to gain a competitive edge.*

*China, which represents the world’s second-largest pharmaceutical market, has targeted its life sciences sector as a key area for strategic growth, singling the industry out in its ‘Made in China 2025’ initiative and undertaking aggressive reforms to shore up its status. With respect to active pharmaceutical ingredients, for instance, China has already established global dominance, and a range of recent reforms have substantially narrowed the country’s lag-times for new drug approvals and launches.*

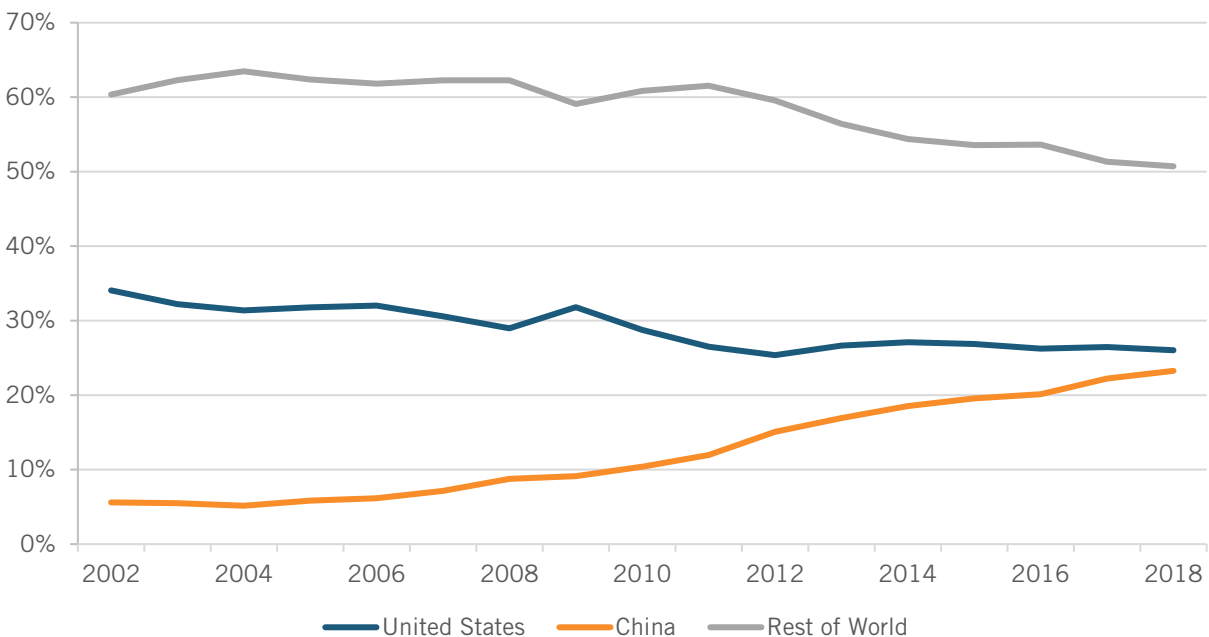
*Meanwhile, the drug price controls included in the Democrats’ tax and spending package would slash domestic life sciences R&D by close to one-fifth in the years ahead, according to a University of Chicago study. In other words, as the Chinese Communist Party works to seize our global biopharmaceutical leadership, we seem poised to weaken our own sector through bureaucratic new mandates.*

- *How do you see price controls like the ones proposed in BBBA as impacting our global life sciences leadership—particularly in relation to China—and what are some of the potential implications—both for medicine and for national security?*

China rejects the foundational WTO principle of *comparative advantage*—that countries should specialize in production of goods and services at which they’re most efficient—and instead seeks *absolute advantage*—dominance, or at least self-sufficiency, in virtually all advanced-technology industries, from aerospace and autos to batteries and biotechnology. That China can quickly achieve these goals is evident from looking at China’s experience in rapidly coming to dominate the global market for production of solar photovoltaic cells. Indeed, China’s global share of production of PV cells, the industry’s core technology, surged from 14 to 60 percent between 2006 and 2013.<sup>102</sup> The massive industrial subsidies China’s government conferred on the industry—at least \$42 billion from 2010 to 2012 alone—played a key role in helping Chinese solar PV prices decrease by 85 percent from 2009 to 2017, knocking out hundreds of foreign competitors in the process. In other words, U.S. policymakers should be under no illusion that U.S. high-tech industries don’t face serious threats of Chinese “innovation mercantilist” practices such as massive industrial subsidization and rampant IP theft.<sup>103</sup>

China certainly has ambitions to likewise become a leading, if not the leading, global player in life-sciences industries. In 2018, China’s value added in the global pharmaceuticals industry was over \$123 billion, 18.5 times its 1995 level and nearly equal to the contribution from the entire European Union.<sup>104</sup> In fact, from 2002 to 2018, China’s share of the world total of global pharmaceutical industry value-added grew over four-fold, from 5.6 to 23 percent, while the United States’ fell from 34 to 26 percent. (See Figure 7.) China has also become the world leader in its share of global research publications in the life-sciences, now accounting for over 70,000 annual biology and biomedicine scientific publications in 2020 and surpassing America’s contribution.<sup>105</sup>

**Figure 7: Country shares of value added in the global pharmaceutical industry, 2002–2018**<sup>106</sup>



Meanwhile, China has become an indispensable player in the production of many active pharmaceutical ingredients (APIs). For instance, by volume, China's share of global exports of tetracycline/doxycycline reached 86 percent in 2020, and 63 percent for vitamin B1.<sup>107</sup> In fact, at least three WHO-identified essential medicines—capreomycin and streptomycin for treatment of Mycobacterium tuberculosis and sulfadiazine, used to treat chancroid and trachoma—rely on API manufacturers based solely in China.<sup>108</sup>

But it's not just APIs; China is increasingly trying to compete at the frontiers of biomedical innovation. For instance, as of mid-2018, 25 Chinese companies had applied for approvals for advanced anticancer drugs based on biotechnology (PD-1/PD-L1 inhibitors).<sup>109</sup> Moreover, in 2017, China had 139 clinical trials with chimeric antigen receptor treatment (CAR-T) cell therapy, compared with around 118 in the United States.<sup>110</sup> Of just over 400 CAR-T clinical trials conducted in March of 2019, 166 were in China, and 165 in the United States.<sup>111</sup>

Foreign IP theft has been a critical component of China's efforts to catch up in the global biotechnology race. Chinese actors have hacked into the IT systems of numerous U.S. biopharmaceutical companies, including Abbott Laboratories and Wyeth (now part of Pfizer).<sup>112</sup> Similarly, a report to the U.S. China Economic and Security Review Commission notes that Ventria Bioscience, GlaxoSmithKline, Dow AgroSciences LLC, Cargill Inc., Roche Diagnostics, and Amgen have all experienced theft of trade secrets or biological materials perpetrated by current or former employees with the intent to sell to a Chinese competitor. And in the academic sector, researchers have stolen information or samples from their employers at Cornell University, Harvard University, and University of California at Davis.<sup>113</sup> China has also issued compulsory licenses for the IP of particular drugs.<sup>114</sup>

In summary, China poses an increasingly serious threat to U.S. innovation leadership in the life-sciences, both from policies that are legitimate (i.e., investing more in R&D or producing more scientific research and researchers) and those that are mercantilist (i.e., pilfering foreign IP or introducing pharmaceutical data exclusivity rules that favor companies that first launch in China).<sup>115</sup> To the extent price controls impede U.S. innovators' abilities to earn revenues to reinvest in future generations of biomedical innovation (as demonstrated here) then the BBBA (like other drug price control proposals) would endanger U.S. biomedical innovation leadership and open the door to foreign competitors.

## **QUESTIONS FOR THE RECORD FROM U.S. SENATOR BEN SASSE**

1. *While we need to rein in the cost of pharmaceuticals, we also need to consider access to and creation of new therapeutics that can be potentially lifesaving. Multiple sclerosis is a good example of a disease that has benefitted from follow-on innovations. In 2020, the FDA approved Novartis' Kesimpta as a treatment for MS. This drug was originally approved 11 years earlier for the treatment of a rare form of leukemia, making this a follow-on product. It is common to find new indications for existing drugs, and we want to incentivize research and development and the multiple clinical trials that make this possible.*
  - *How would some of the lesser discussed policies in Build Back Better actually create disincentives to finding new indications for existing drugs? For example, wouldn't the bill make tax changes that disincentivize finding new indications for orphan drugs?*

- *Can you speak to how costly the clinical trial process is, and how this might drive up prices? For example, testing a new indication for Kesimpta took 10 years and spanned 350 sites across 37 countries. This was for a drug that already existed and was approved for another use.*
  - *How might we reform this process to decrease costs?*
- *Multiple Sclerosis unfortunately lacks a cure. How would the price controls being suggested by Democrats hurt efforts to find a cure for MS?*

As noted in ITIF’s written testimony, a wide variety of academic studies, over time and across nations and international organizations, find that drug price controls impede biomedical innovation. Indeed, virtually all academic studies consistently reveal that a reduction in current drug revenues leads to a decrease in future research and the number of new drug discoveries.<sup>116</sup> The Build Back Better Act’s drug price control policies would introduce the same effect.

2021 research by Tomas Philipson and Troy Durie at the University of Chicago estimate that a 1 percent reduction in pharmaceutical industry revenue leads on average to a 1.54 percent decrease in R&D investment.<sup>117</sup> Applying their research to HR 5376 (the Build Back Better Act), Philipson and Durie find the legislation would reduce revenues by 12.0 percent through 2039, with the reduced revenues meaning R&D spending would fall by about 18.5 percent, or \$663 billion. They find that this cut in R&D activity would lead to 135 fewer new drugs, with this drop in new drugs is predicted to generate a loss of 331.5 million life years in the United States.<sup>118</sup> The authors further find that therapies that treat diseases of the endocrine, cardiovascular, and respiratory systems along with treatments for cancer and neurological diseases would be most impacted by the BBBA’s policies because they make up a high share of Medicare spending.<sup>119</sup>

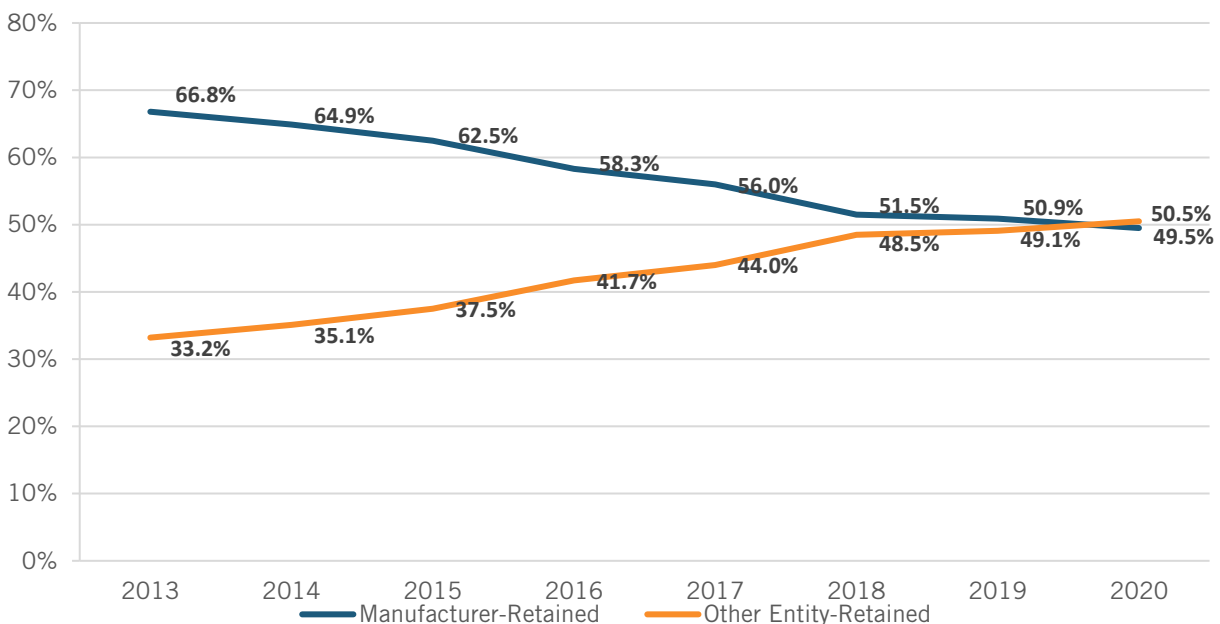
Just as in other areas of life-sciences innovation, U.S. companies lead the way in innovating solutions for rare, or orphan, diseases. That’s in large part because, in 1983, Congress introduced the Orphan Drug Act (ODA) and its Orphan Drug Tax Credit (ODTC), a federal tax credit available to pharmaceutical companies working to find cures for certain rare diseases that affect patient populations of fewer than 200,000 individuals.<sup>120</sup> There are approximately 7,000 rare diseases, the majority of which are genetic in nature and which affect between 25 and 30 million Americans, although approximately 95 percent have no effective treatment.<sup>121</sup> To incent R&D of drugs for such diseases, Congress set the ODTC equal to 50 percent of qualified clinical trial costs (and also offered a seven-year period of orphan drug exclusivity). Since the law’s enactment, over 500 orphan products have been approved by the U.S. FDA, whereas prior to the law’s introduction fewer than 40 drugs were approved in the United States to treat rare diseases and on average only two new orphan drugs were produced each year.<sup>122</sup> A 2015 study by the National Organization for Rare Disorders (NORD) found that at least one-third fewer new orphan drugs would have been developed to treat rare diseases over the preceding 30 years had the act not been implemented.<sup>123</sup> Indeed the ODA has been widely regarded as a success, as over 600 orphan drugs have been approved since the passage of the ODA, in contrast to fewer than 10 medicines for rare diseases in the decade prior to its enactment.<sup>124</sup>

Unfortunately, provisions in the BBBA would likely be deleterious for rare disease innovation As Peter Saltonstall, CEO and President of The National Organization for Rare Disorders (NORD), elaborates:

Section 138141 of the *Build Back Better Act* would dramatically curtail the Orphan Drug Tax Credit for qualified clinical testing expenses by removing this critical incentive for all but the first approved orphan use of a new drug. The ODTX was already diminished in 2017 in the *Tax Cut and Jobs Act* when Congress reduced the total amount of the tax credit for qualifying clinical testing expenses from 50% to 25%. Given the significant time it takes to conduct clinical trials, the full impact of the changes made by the 2017 law are still unknown. To further reduce availability of the tax credit will hurt rare disease patients and hinder their ability to access treatments found to be safe and effective to treat their specific condition.<sup>125</sup>

The question about multiple sclerosis, and the one which follows regarding insulin prices, should focus policymakers’ attention on the increasingly distortive roles that PBMs and other actors in the pharmaceutical supply chain are causing for U.S. drug prices. As ITIF noted in its written testimony, over time, drug manufacturers have lost a growing share of drug expenditures to other members of the drug supply chain, such as PBMs, health plans, hospitals, the government, and pharmacies. Since 2013, the share of drug expenditures going to manufacturers has decreased by 13 percent. Thus, while total expenditures on brand drugs grew by \$268 billion between 2013 and 2020, only 31 percent of the increase accrued to manufacturers, while 69 percent accrued to other stakeholders. By 2020—for the first time ever—over half of drug expenditures accrued to non-manufacturers. (See Figure 8.)

**Figure 8: Total gross expenditures for brand medicines received by manufacturers and other stakeholders (2013–2020)<sup>126</sup>**



That matters, because when patients go to the pharmacy, they’re likely buying their medications from one of three pharmacy benefit managers—middlemen insurance companies that determine the final out-of-pocket



cost for our medicines. In fact, just three PBMs—Caremark, Express Scripts, and OptumRx—control 76 percent of all prescription drug formularies in the United States.<sup>127</sup>

Incidentally, this is actually a marketplace where there is significant concentration, unlike the pharmaceutical industry, as has been asserted by Congressmembers such as Senator Elizabeth Warren and Representative Katie Porter, the latter who cites data asserting that “between 1995 and 2015, 60 pharmaceutical companies merged into just 10.”<sup>128</sup> But rather, the reality is that considering the combined output for firms in the United States (not imports), the sales for the top four in each industry (C4 ratio) in the Pharmaceutical Preparation Manufacturing and Biological Product Manufacturing industries (NAICS codes 325412 and 325414) increased only modestly from 2002 to 2017, from 36 percent to 43 percent, while the C8 ratio increased from 54 to 58 percent, and the C20 ratio fell slightly from 77 percent to 76 percent.<sup>129</sup> In other words, the top 20 firms in this sector have the same market share as the three leading PBMs.

Unfortunately, the PBM system has been designed in a way that is the opposite of what was originally intended: PBMs helping to lower drug costs at the pharmacy counter. Consider the case of Tecfidera (dimethyl fumarate), a blockbuster multiple sclerosis treatment manufactured by Biogen which went generic in late 2020. Within months of Tecfidera going off-patent, more than ten generic drug makers brought competing versions of dimethyl fumarate to market with “deeply discounted prices to Tecfidera.”<sup>130</sup> Roughly one year post-generic launch, aggressive competition from generics manufacturers drove prices for a 60-count bottle of the generic equivalent today down to “a 99%+ discount to the brand’s list price.”<sup>131</sup> However, by Q3 2021, Medicare Part D plans covering the majority of U.S. seniors didn’t even make the generic equivalent available to their members, instead only offering them brand-name Tecfidera.<sup>132</sup> Moreover, when the generic was made available to seniors, it was largely done so at “negotiated prices” that far exceeded the lowest cost generic equivalent’s.<sup>133</sup>

In other words, here’s a case where America’s life-sciences innovation system worked to support creation of an innovative drug and then a subsequent pathway for entry of much-lower-priced generic drugs, but it was the middleman system that prevented the cheaper drugs from being made available to seniors. Policymakers need to take a much closer look at the role of PBMs in America’s drug payment system. That’s why ITIF supports proposals calling for the imposition of greater fiduciary obligations on the activities of PBMs. ITIF also supports other proposals to increase drug price transparency, including removal of pharmacy gag clauses and requiring plan sponsors to provide patients information about drug price increases and lower cost-options.<sup>134</sup>

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>135</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>136</sup>

In addition to innovative ways to enhance drug R&D efficiency, policymakers can also work to enhance drug production efficiency. For instance, One study contends that pharmaceutical manufacturing is expensive, inefficient, and non-innovative, with firms using outdated production techniques and old plants.<sup>137</sup> The study estimates modern biomanufacturing techniques could eliminate as much as \$50 billion in annual production costs.

To address this, Congress should significantly expand funding for biomedical Manufacturing USA centers, including expanding funding for The National Institute for Innovation in Manufacturing Biopharmaceuticals (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>138</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>139</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>140</sup>

## **QUESTIONS FOR THE RECORD FROM U.S. SENATOR JOHN BARRASSO**

1. *As a doctor, I have seen firsthand the value innovative medicines provide to folks across Wyoming. When we make policy here in Washington, it is critical we preserve the incentives for cutting-edge therapies to come to market so folks can live longer and healthier lives.*

*That being said, I have concerns about the high list prices - particularly for long-established drugs. Insulin is one example. This is a life-saving drug that has been part of medical practice for decades.*

*Though negotiated discounts and rebates can reduce the net price for drugs like insulin, some patients' copays continue to climb as list prices tick higher.*

- ***What are the best solutions to lower the price patients pay at the pharmacy counter for insulin?***

First, it's important to recognize that most Americans are able to access their insulin at affordable prices. In fact, 76 percent of U.S. insulin prescriptions cost patients less than \$35 out of pocket.<sup>141</sup> In fact, across all patients, the average out-of-pocket cost per month for an insulin prescription was \$31 in 2019. Companies also offer affordable subscription plans for diabetic patients, such as Novo Nordisk's My\$99Insulin plan, whereby eligible patients pay \$99 for a monthly supply of any combination of Novo Nordisk insulin products.<sup>142</sup>

However, there are certainly cases where patients are paying too much for insulin. Indeed, while just 24 percent of insulin prescriptions cost patients more than \$35 out of pocket, these prescriptions account for 82 percent of total patient spending on insulin.<sup>143</sup> For this reason, as noted in its testimony, ITIF supports capping monthly patient out-of-pocket costs for drugs treating certain chronic diseases, such as a \$35 monthly cap for insulin for the treatment of diabetes.<sup>144</sup>

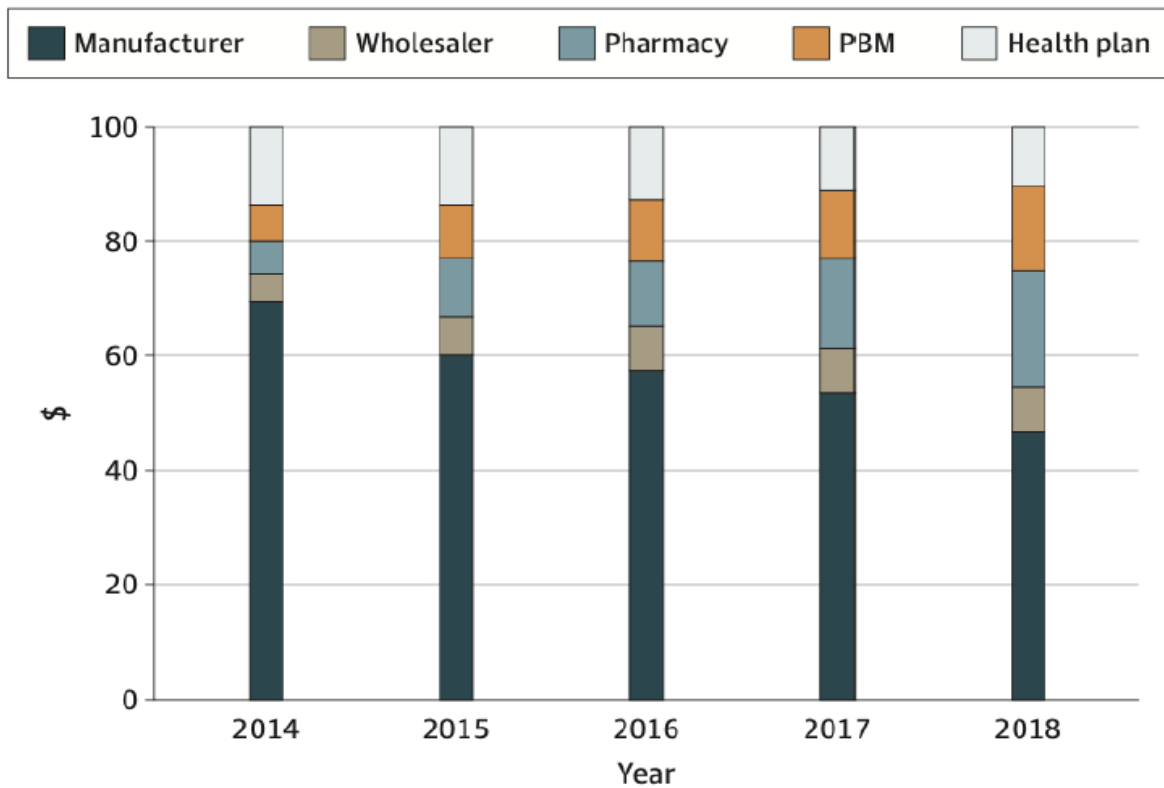
However, the more fundamental issue, for insulin or many other drugs, is that the rebates insurers and PBMs negotiate for Medicare Part D drugs need to be passed through to seniors at the pharmacy counter. The rebates (averaging nearly 30 percent for Medicare Part D drugs) are usually paid to PBMs in consideration of preferred placement on the insurance plan's formulary, but the PBMs tend not to share the rebates directly with beneficiaries. Changing this rule change could save older Americans as much as \$83 billion at the pharmacy counter over the span of 10 years.<sup>145</sup>

Indeed, until the rebate system is fundamentally reformed, list prices are going to continue to increase at rates well above the actual cost of drugs, with insulin a prime example. For instance, a bipartisan report by the Senate Finance Committee found that some PBMs have secured rebates on insulin as high as 70 percent in recent years.<sup>146</sup> In fact, in 2019, PBMs paid \$52 for an insulin product that had a list price of more than \$350.<sup>147</sup> Manufacturers often sell insulin, an essential medicine, to insurers and PBMs at deep discounts. However, many patients are forced to make out-of-pocket payments based on insulin's irrelevant list price.<sup>148</sup> For instance, one study found that list prices for Sanofi's insulins have grown by 140 percent over the past eight years, while net prices have declined by 41 percent.<sup>149</sup> Similarly, over the past five years, the list price of Eli Lilly's Humalog insulin increased by 27 percent, while its net price declined by 10 percent.<sup>150</sup> But as Adam Fein notes, [formulary plan] "benefit designs often mask these declining net prices." As Fein notes, "Payers' drug costs and manufacturers' revenues have been dropping for the past four years. Despite this decline, patients' out-of-pocket costs have been rising."<sup>151</sup> As Fein concludes, "Third-party payers' benefit designs remain a significant barrier to addressing drug costs. Many continue to use the ever-growing rebate dollars of the gross-to-net bubble to offset overall plan costs rather than reducing patient's out-of-pocket spending."<sup>152</sup>

As the Biotechnology Innovation Organization (BIO) writes:

The vertical consolidation of pharmacy services paired with relatively few competitors in the space has led to some markets which exhibit monopsonist characteristics—the PBMs can represent the sole purchaser of prescription drugs for a majority of covered lives, employer plans or fully insured commercial products may have few (or no) alternatives to the dominate PBM(s) in their market if they wanted to seek out another entity to manage their pharmacy benefit, and the complexity of the pharmaceutical supply chain and scale that existing PBMs can leverage represent significant barriers for new entrants.<sup>153</sup>

**Figure 9: Average distribution of \$100 in insulin expenditures for 32 insulin products across distribution system participants, 2014–2018<sup>154</sup>**



A recent study analyzed the hypothetical distribution of \$100 of spending on 32 insulin products across manufacturers, insurers, and other supply chain entities from 2014 to 2018. The authors found that while expenditures per 100 units of insulin changed little over this time, the distribution of spending changed significantly. Over this period, the share of spending retained by insulin manufacturers and health plans fell (by 33 percent and 24.7 percent, respectively), while the amounts retained by supply chain intermediaries increased substantially: wholesalers (74.7 percent), pharmacies (228.8 percent), and PBMs (154.6 percent).<sup>155</sup> (See Figure 9.)

Indeed, America’s current drug reimbursement system can lead health plans and PBMs to favor medicines with high list prices and large rebates, making them reluctant to include lower-cost insulin and authorized generics on formularies. In fact, one study found that just one in four Medicare Part D beneficiaries, and one in five patients with commercial insurance, have access to lower-price authorized generic insulin through insurance.<sup>156</sup> That study finds that sharing negotiated rebates would lower Medicare Part D costs for patients,

estimating that for a prototypical Medicare Part D patient with diabetes taking five medicines overall (including insulin), passing through those rebates would reduce their out-of-pocket spending by nearly \$900 annually, while only increasing premiums \$3 to \$6 per month.<sup>157</sup>

2. *Before coming to the Senate I practiced orthopedic surgery of over twenty years. During my surgical training, I got to know many patients with Duchenne muscular dystrophy. These young boys and their families made a lasting and personal impact on me. The sad fact was when I practiced medicine, there were no approved treatments for Duchenne's. This is why I helped host the Jerry Lewis telethon in Wyoming for many years.*

*In fact, the first FDA approved treatment for Duchenne's did not become available until well after I joined the Senate in 2016. For families impacted by Duchenne's, this first approval was a beacon of hope. Now, thanks to American scientific innovation, there are multiple FDA approved therapies for Duchenne's. We have not cured this disease, but we are making important progress.*

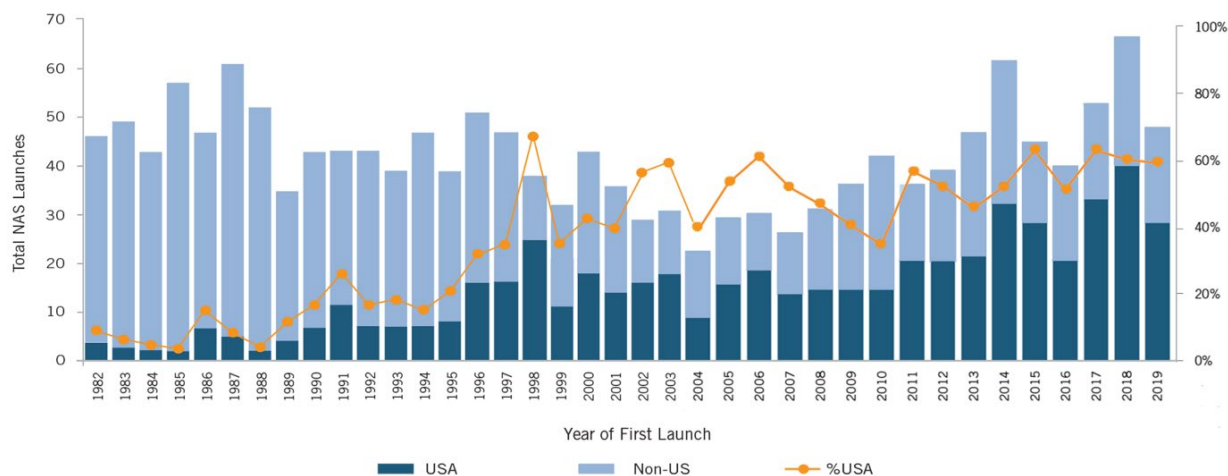
*As a doctor, I am passionate about ensuring the progress continues. According to the Food and Drug Administration, there are over 7,000 rare diseases that impact over 30 million Americans. While we all want to lower the price of prescription drugs, we must ensure patients can access the next generation of life changing medications.*

- ***Can you please discuss the importance of maintaining investments in scientific research, especially with regard to supporting investments in therapies that address conditions that impact smaller patient populations?***

As noted, the United States leads the world in biomedical innovation. In fact, over the past 20 years, more than 60 percent of all new drugs worldwide have been created in the United States—more than in the rest of the world combined.<sup>158</sup> That's in no small part because the United States has clearly been the world's largest global funder of biomedical R&D investment over the past two decades, a share that some analyses suggested reached as high as 70 to 80 percent over that time period.<sup>159</sup> Indeed, there's a direct link between the United States being the world's leading investor in biomedical R&D and the world's leading producer of innovative drugs.

And, again, it's important to remember that this wasn't always the case. Indeed, the United States once was a global "also-ran" in biomedical innovation: Europe was once the world's pharmaceuticals industry leader. Between 1960 and 1965, European-headquartered companies invented 65 percent of the world's new drugs, and in the latter half of the 1970s, European-headquartered enterprises introduced more than twice as many new drugs to the world as did U.S.-headquartered enterprises (149 to 66).<sup>160</sup> In fact, throughout the 1980s, fewer than 10 percent of new drugs were introduced first in the United States.<sup>161</sup> (See Figure 10.)

**Figure 10: U.S. share of new active substances launched on the world market, 1982–2019<sup>162</sup>**



And, as recently as 1990, the industry invested 50 percent more in Europe than in the United States.<sup>163</sup> As Shanker Singham of the Institute of Economic Affairs notes, “Europe was the unquestioned center of biopharmaceutical research and development for centuries, challenged only by Japan in the post-war period.”<sup>164</sup> As of 1990, European and U.S. companies each held about a one-third share of the global drug market.

As Nathalie Moll of the European Federation of Pharmaceutical Industries and Associations (EFPIA) wrote in January 2020:

The sobering reality is that Europe has lost its place as the world’s leading driver of medical innovation. Today, 47 percent of global new treatments are of U.S. origin compared to just 25 percent emanating from Europe (2014–2018). It represents a complete reversal of the situation just 25 years ago.”<sup>165</sup>

By 2014, nearly 60 percent of new drugs launched in the world were first introduced in the United States, an indication both that more were being invented in the United States and that drug companies from Europe and elsewhere were introducing new drugs in America first because that’s where they could recoup their investments.

This dramatic shift away from Europe serving as the “world’s medicine cabinet” did not happen principally due to deficient corporate strategy or management. Instead, poor public policy in Europe and superior policy in the United States made the difference. This was particularly the case when it came to drug price controls. As one report explained in 2002, “the heart of pharma’s problem in Europe is the market’s inability to ‘liberate the value’ from its products.”<sup>166</sup> This was a reference to the “complex maze of government-enforced pricing and reimbursement controls” that “depressed pharma prices to the point where some companies now believe it is just not economical to launch new products in certain European countries.”<sup>167</sup>

Europe offers a case study of the damage drug price controls inflict on the competitiveness of a nation’s biopharmaceutical industry. The United States should not follow its path. Uniquely, the United States leads

the world in innovating new drug and getting them to patients first while sustaining a globally competitive industry and over time making drugs broadly affordable in incentivizing competition and creating generic pathways. Policymakers should seek to improve upon this system where necessary (as ITIF noted in its testimony) but wholesale changes in the form of stringent drug policies are not needed nor warranted.

3. *The proposals put forward by Congressional Democrats ignore the real challenge of ensuring that generics and biosimilars are able to launch and gain adoption quickly.*

*As a doctor, I strongly support both generics and biosimilars because I know they provide the same benefits as the branded products, but often at a much lower price.*

- ***What do you believe will be the impact of the policies in Build Back Better, specifically regarding the adoption and development of future generics and biosimilar medications?***

They will be delirious. Please see the response offered previously to Senator Crapo's question.

## Endnotes

---

1. Scott Brown, "Dairy price inflation lags other foods," *Hoard's Dairyman*, February 17, 2022, <https://hoards.com/article-31538-dairy-price-inflation-lags-other-foods.html>.
2. Bureau of Labor Statistics, Consumer Price Index (accessed March 10, 2022) <https://www.bls.gov/cpi/>.
3. Bureau of Labor Statistics, Consumer Expenditure Survey (Healthcare expenditures, 2005-2020) <https://www.bls.gov/cex/>.
4. Ibid.
5. Peterson Center on Healthcare and Kaiser Family Foundation, Peterson-KFF Health System Tracker, "National Health Spending Explorer," <https://www.healthsystemtracker.org/health-spending-explorer/>.
6. Peterson-KFF Health Systems Tracker, (National Health Spending, accessed March 12, 2022), <https://www.healthsystemtracker.org/health-spending-explorer/>.
7. Altarum, "Projections of the Non-Retail Prescription Drug Share of National Health Expenditures," September 2020, 3, <https://altarum.org/publications/projections-non-retail-prescription-drug-share-national-health-expenditures>; Inmaculada Hernandez et al., "Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the US, 2007-2018," *Journal of the American Medical Association* Vol. 323, No. 9 (2020): 856, <https://pubmed.ncbi.nlm.nih.gov/32125403/>.
8. Doug Holtz-Eakin, "Testimony on: The Build Back Better Act's Prescription Drug Policies and Their Potential Impacts," (American Action Forum, March 16, 2022), 5-6, 12, <https://www.finance.senate.gov/imo/media/doc/DHE%20SFC%20Testimony%20BBBA%20Drug%20Policies.pdf>.
9. Ibid., 6, 12.
10. Ulrik Boesen, "Why the Medical Device Tax Should Be Repealed" Fiscal Fact No. 677, (Tax Foundation, November 2019), 1, [https://files.taxfoundation.org/20191203103452/TaxFoundation\\_FF677.pdf](https://files.taxfoundation.org/20191203103452/TaxFoundation_FF677.pdf).
11. Department of Health and Human Services, Centers for Medicare & Medicaid Services, Office of the Actuary, "Estimated Financial Effects of the "Patient Protection and Affordable Care Act," as Amended," April 22, 2010, [https://www.cms.gov/Research-Statistics-Data-and-Systems/Research/ActuarialStudies/downloads/PPACA\\_2010-04-22.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Research/ActuarialStudies/downloads/PPACA_2010-04-22.pdf).
12. Boesen, "Why the Medical Device Tax Should Be Repealed."
13. Stephen Ezell, "Affordable Care Act Endangers Innovative U.S. Life Sciences Industries," *Innovation Files*, July 3, 2013, <https://www.innovationfiles.org/affordable-care-act-endangers-innovative-u-s-life-sciences-industries/>.
14. James R. Hagerty, "When Nixon Froze Prices, Arnold Weber Enforced the Rules," *The Wall Street Journal*, August 27, 2020, <https://www.wsj.com/articles/when-nixon-froze-prices-arnold-weber-enforced-the-rules-11598536800>.
15. William N. Walker, "Nixon Taught Us How Not to Fight Inflation," *The Wall Street Journal*, August 13, 2021, <https://www.wsj.com/articles/nixon-fight-inflation-price-controls-stagflation-gas-shortages-biden-democrats-reconciliation-bill-federal-reserve-11628885071>.
16. Congressional Budget Office (CBO), "Research and Development in the Pharmaceutical Industry" (CBO, April 2021), 4-5, <https://www.cbo.gov/publication/57025>.
17. Ibid.
18. TEconomy Partners, LLC and PhRMA, "Economic Impact of the U.S. Biopharmaceutical Industry," (TEconomy Partners and PhRMA, December 2019), 7, <https://www.phrma.org/>



---

/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/D-F/Economic-Impact-US-Biopharmaceutical-Industry-December-2019.pdf.

19. Congressional Budget Office, “Research and Development in the Pharmaceutical Industry.”
20. Ibid.
21. Beth Snyder Bulik, “The top 10 ad spenders in Big Pharma for 2020” *FiercePharma*, April 19, 2021, <https://www.fiercepharma.com/special-report/top-10-ad-spenders-big-pharma-for-2020>.
22. Robert D. Atkinson, “Why Life-Sciences Innovation Is Politically “Purple”—and How Partisans Get It Wrong” (ITIF, February 2016), 6, <https://itif.org/publications/2016/02/22/why-life-sciences-innovation-politically-purple>.
23. D. L. Frosch, D. Grande, D.M. Tarn., and R. L. Kravitz, “A Decade of Controversy: Balancing Policy with Evidence in the Regulation of Prescription Drug Advertising” *American Journal of Public Health* Vol. 100, No. 1 (January 2010): 24–32, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2791253/>.
24. Ibid., 5.
25. Neeraj Sood, et al., “Do companies in the pharmaceutical supply chain earn excess returns?” *International Journal of Health Economics and Management* Vol. 21 (January 4, 2021): 99–114, <https://doi.org/10.1007/s10754-020-09291-1>. (The researchers calculated the “risk adjusted rate of return” by subtracting capital costs, which vary with the level of risk across industries.)
26. Ibid., 110.
27. Frank Lichtenberg, “Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000–2009” *Health Policy and Technology* Vol. 3, Issue 1 (March 2014): 36–58, <https://www.sciencedirect.com/science/article/abs/pii/S2211883713000646>.
28. TEconomy Partners, LLC and PhRMA, “Economic Impact of the U.S. Biopharmaceutical Industry,” 7.
29. PhRMA, “Chart Pack: Biopharmaceuticals in Perspective, Fall 2020” (PhRMA, 2020), 21, <https://www.phrma.org/resource-center/Topics/Advances-in-Treatment/Chart-Pack-Biopharmaceuticals-in-Perspective-Fall-2020>
30. Ibid., 22.
31. PhRMA, “Why Has Research Into Alzheimer's Disease Been So Hard?” <https://innovation.org/en/diseases/neurological/alzheimers/why-has-research-into-alzheimers-disease-been-so-hard>.
32. The Alzheimer’s Association, “Changing the Trajectory of Alzheimer’s Disease” (The Alzheimer’s Association, 2015), [http://www.alz.org/documents\\_custom/trajectory.pdf](http://www.alz.org/documents_custom/trajectory.pdf).
33. Chi Heem Wong, Kien Wei Siah, and Andrew W. Lo, “Estimation of clinical trial success rates and related parameters” *Biostatistics* Vol. 20, Issue 2 (April 2019): 273–286, <https://doi.org/10.1093/biostatistics/kxx069>.
34. BIO, “COVID-19 Therapeutic Development Tracker,” <https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker>; BIO, “Response to Federal Trade Commission: Request for Information on Merger Enforcement,” (BIO, April 15, 2022), 4.
35. FDA CDER, “Novel Drug Approvals for 2020,” (January 13, 2021), <https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2020>.
36. Jeff Craven, “FDA approved more first-in-class drugs, gave more accelerated approvals in 2021,” Regulatory Affairs Professional Society, (January 27, 2022), <https://www.raps.org/news-and-articles/news-articles/2022/1/fda-approved-more-first-in-class-drugs-more-with-a>.
37. FDA CBER, “2020 Biological License Application Approvals,” (August 20, 2020), <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2020-biological-license-application-approvals>.

- 
38. Kari Oakes, “In 2020, all goal dates met for CDER’s novel approvals,” (January 13, 2021), <https://www.raps.org/news-and-articles/news-articles/2021/1/in-2020-all-goal-dates-met-for-cders-novel-approva>.
  39. FDA CDER, “Novel Drug Approvals for 2021,” (January 6, 2022), <https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2021>; FDA CBER, “2021 Biological License Application Approvals,” (December 20, 2021), <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2021-biological-license-application-approvals>.
  40. Craven, “FDA approved more first-in-class drugs, gave more accelerated approvals in 2021.”
  41. FDA CDER, “Novel Drug Approvals for 2021,” (March 28, 2022), <https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2022>; FDA CBER, “2021 Biological License Application Approvals,” (March 16, 2022), <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2022-biological-license-application-approvals>; Drugs.com, “New Drug Approvals,” (accessed April 21, 2022), <https://www.drugs.com/newdrugs.html>.
  42. *In Vivo: The Business and Medicine Report* Vol. 34, No. 1 (January 2016), 25, <https://invivo.pharmaintelligence.informa.com/outlook/industry-data-/media/marketing/Outlook%202019/pdfs/2016.PDF>.
  43. Ashley Mullard, “2019 FDA Drug Approvals” *Nature Reviews: Drug Discovery* Vol. 19 (February 2020): 79, <https://www.nature.com/articles/d41573-020-00001-7>.
  44. Office of Congresswoman Katie Porter, “Killer Profits: How Big Pharma Takeovers Destroy Innovation and Harm Patients” (January 2021), 6, [https://porter.house.gov/uploadedfiles/final\\_pharma\\_ma\\_and\\_innovation\\_report\\_january\\_2021.pdf](https://porter.house.gov/uploadedfiles/final_pharma_ma_and_innovation_report_january_2021.pdf).
  45. Rena Conti, “Statement of Rena Conti: Prescription Drug Spending Reform Will Not Harm Innovation and Will Benefit the American Public at Senate Finance Committee Hearing Prescription Drug Price Inflation: An Urgent Need to Lower Drug Prices in Medicare,” March 16, 2022, 6, <https://www.finance.senate.gov/imo/media/doc/Conti%20SFC%20Final%20Testimony.pdf>.
  46. Mark Robberson, “An Empirical Analysis of Innovation in the Pharmaceutical Industry by Drug Class: Implications for Regulatory Policy” (Johns Hopkins Bloomberg School of Public Health, submitted for the 2019 Center of Excellence in Regulatory Science and Innovation & Master of Science in Regulatory Science and Food Safety Regulation), <https://www.jhsph.edu/research/centers-and-institutes/center-of-excellence-in-regulatory-science-and-innovation/Mark%20Robberson%20CERSI%20paper%2020190505.pdf>.
  47. Augustus John Rush and David J. Kupfer, “Strategies and tactics in the treatment of depression,” in *Treatment of Psychiatric Disorders*, edited by G. O. Gabbard (Washington, D.C.: American Psychiatric Publishing, 2001).
  48. Joseph A. DiMasi and Laura B. Faden, “Competitiveness in Follow-On Drug R&D: A Race or Imitation?” *Nature Reviews Drug Discovery* Vol. 10, No. 1 (January 2011), <http://www.nature.com/nrd/journal/v10/n1/abs/nrd3296.html>.
  49. Ibid.
  50. United States Government Accountability Office (GAO), *DRUG INDUSTRY: Profits, Research and Development Spending, and Merger and Acquisition Deals* (GAO, November 2017), <https://www.gao.gov/assets/gao-18-40.pdf>.
  51. Jocelyn Mason and Kimberly D. Boeser, “The changing HCV treatment cascade,” *Infectious Disease News*, October 2017, <https://www.healio.com/infectious-disease/hepatitis-c/news/print/infectious-disease-news/{87b74536-f358-43d3-a804-f37a98402b0b}/the-changing-hcv-treatment-cascade>.
  52. Holtz-Eakin, “Testimony on: The Build Back Better Act’s Prescription Drug Policies and Their Potential Impacts,” 11.

- 
53. Ibid., 8.
  54. Tomas J. Philipson and Troy Durie, “Issue Brief: The Impact of HR 5376 on Biopharmaceutical Innovation and Patient Health” (The University of Chicago, November 9, 2021), 20, <https://cpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2021/08/Issue-Brief-Drug-Pricing-in-HR-5376-11.30.pdf>.
  55. John Wu and Robert D. Atkinson, “How Technology-Based Start-Ups Promote U.S. Economic Growth,” (ITIF, November 2017), 12, <https://itif.org/publications/2017/11/28/how-technology-based-start-ups-support-us-economicgrowth>.
  56. Biotechnology Innovation Organization (BIO), “Research & Development: Biopharmaceutical Sector, A Driver of Innovation,” [https://www.bio.org/sites/default/files/legacy/bioorg/docs/BIO\\_RD\\_one%20pager%205-9-17.pdf](https://www.bio.org/sites/default/files/legacy/bioorg/docs/BIO_RD_one%20pager%205-9-17.pdf); CBO, “Research and Development in the Pharmaceutical Industry,” 8.
  57. Pierre Dubois, “Market size and pharmaceutical innovation,” *The Rand Journal of Economics* Vol. 46, Issue 4 (October 2015): 844–871, <https://onlinelibrary.wiley.com/doi/full/10.1111/1756-2171.12113>.
  58. Destrina Grace Simanjuntak and Raymond R. Tjandrawinata, “Impact of Profitability, R&D Intensity, and Cash Flow on R&D Expenditure in Pharmaceutical Companies” (Social Science Research Network, April 29, 2011), [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=1824267](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1824267).
  59. Alfonso Gambardella, *Science and Innovation: The US Pharmaceutical Industry During the 1980s* (Cambridge University Press, 1995).
  60. R. Henderson and I.M. Cockburn, “Scale, Scope, and Spillovers: The Determinants of Research Productivity in the Pharmaceutical Industry” *RAND Journal of Economics* Vol. 27, No. 1 (1996): 32-59, <https://www.nber.org/papers/w4466>.
  61. Nicole Longo, “Five reasons tying VA prices to Medicare Part D misses the mark,” *The Catalyst*, September 22, 2021, <https://catalyst.phrma.org/five-reasons-tying-va-prices-to-medicare-part-d-misses-the-mark>.
  62. AmerisourceBergen, “Potential Access Implications of a National Formulary in Part D,” July 16, 2020, <https://www.xcenda.com/insights/comparing-the-generosity-of-drug-coverage-in-the-medicare-part-d-and-veterans-affairs-programs>.
  63. GAO, “Prescription Drugs: Department of Veterans Affairs Paid About Half as Much as Medicare Part D for Selected Drugs in 2017” (GAO, December 2020), <https://www.gao.gov/assets/gao-21-111.pdf>.
  64. Kevin Stroupe et al., “Medication acquisition across systems of care and patient-provider communication among older veterans” *Am J Health Syst Pharm* Vol. 70, Issue 9 (May 2013): 804-13, <https://pubmed.ncbi.nlm.nih.gov/23592363/>.
  65. Pacific BioLabs, “Stages of Drug Development,” <https://pacificbiolabs.com/stages-of-drug-development>.
  66. PhRMA, “Chart Pack: Biopharmaceuticals in Perspective, Summer 2019” (PhRMA, 2019), [https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRMA\\_2019\\_ChartPack\\_Final.pdf](https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRMA_2019_ChartPack_Final.pdf).
  67. Hernandez et al., “Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the US, 2007-2018.”
  68. Ibid., 27.
  69. Jared S. Hopkins and Peter Loftus, “Flip the Script: Drugmakers Blame Middlemen for Price Increases,” *The Wall Street Journal*, February 5, 2019, <https://www.wsj.com/articles/flip-the-script-drugmakers-blame-middlemen-for-price-hikes-11549364401>.
  70. Ibid.

- 
71. Aaron Vandervelde and Eleanor Blalock, “The Pharmaceutical Supply Chain: Goss Drug Expenditures Realized by Stakeholders” (Berkeley Research Group, 2017), [https://www.thinkbrg.com/media/publication/863\\_Vandervelde\\_PhRMA-January-2017\\_WEB-FINAL.pdf](https://www.thinkbrg.com/media/publication/863_Vandervelde_PhRMA-January-2017_WEB-FINAL.pdf).
  72. Robert Zirkelbach, “The PBM story you haven’t heard: Hidden fees quadrupled in two years,” *The Catalyst*, March 20, 2019, <https://catalyst.phrma.org/the-pbm-story-you-havent-heard-hidden-fees-quadrupled-in-two-years>.
  73. Ibid.
  74. Ranjana Chakravarthy et al., “Public- and Private-Sector Contributions to the Research and Development of the Most Transformational Drugs in the Past 25 Years: From Theory to Therapy,” *Therapeutic Innovation and Regulatory Science* Vol. 50, No. 6 (July 2016), <https://www.ncbi.nlm.nih.gov/pubmed/30231735>.
  75. Sabarni K. Chatterjee and Mark L. Rohrbaugh, “NIH Inventions Translate Into Drugs and Biologics With High Public Health Impact” *Nature Biotechnology* 32 (2014): 56, <https://www.nature.com/articles/nbt.2785?message-global=remove>.
  76. Dean Baker, “Malpractice” (Center for Economic Policy Research (CEPR), May/June 2009), <http://cepr.net/publications/op-eds-columns/malpractice>.
  77. Mike Masnick, “Senator Sanders Introduces Medical Innovation Prize Bills,” *TechDirt*, June 1, 2011, <https://www.techdirt.com/2011/06/01/senator-sanders-introduces-medical-innovation-prize-bills/>.
  78. Philip Stevens and Stephen Ezell, “Delinkage Debunked: Why Replacing Patents With Prizes for Drug Development Won’t Work” (ITIF, February 2020), <https://itif.org/publications/2020/02/03/delinkage-debunked-why-replacing-patents-prizes-drug-development-wont-work>.
  79. Matej Mikulic, “Total global spending on pharmaceutical research and development from 2010 to 2024,” Statista, January 23, 2020, <https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/>.
  80. Catherine Saez, “Health R&D Still Underfunded—WHO Members Concerned, NGOs Call For More Ambition,” *IP Watch*, May 29, 2017, <https://www.ip-watch.org/2017/05/29/health-rd-still-underfunded-members-concerned-ngos-call-ambition/>
  81. Ibid.
  82. World Health Organization, “Identification of Health R&D Demonstration Projects,” [http://www.whogis.com/phi/implementation/phi\\_gtc\\_meeting/en/](http://www.whogis.com/phi/implementation/phi_gtc_meeting/en/).
  83. Daniel Spulber, “Public Prizes Versus Market Prices: Should Contests Replace Patents?” *Journal of the Patent and Trademark Office Society* Vol. 97, Issue 4 (2015): 690–735, <https://www.scholars.northwestern.edu/en/publications/public-prizes-versus-market-prices-should-contests-replace-patent>.
  84. Stephen Ezell, “The Bayh-Dole Act’s Vital Importance to the U.S. Life-Sciences Innovation System” (ITIF, March 2019), <https://itif.org/sites/default/files/2019-bayh-dole-act.pdf>.
  85. Lou Berneman, “There are unintended costs of federal efforts to control drug prices,” *PennLive*, March 26, 2022, <https://www.pennlive.com/opinion/2022/03/there-are-unintended-costs-of-federal-efforts-to-control-drug-prices-opinion.html>.
  86. Ibid.; Association of University Technology Managers (AUTM), “Driving the Innovation Economy: Academic Technology Transfer in Numbers,” <https://autm.net/AUTM/media/Surveys-Tools/Documents/FY20-Infographic.pdf>.
  87. John R. Thomas, “March-In Rights Under the Bayh-Dole Act” (Congressional Research Service, August 2016), 7, <https://fas.org/sgp/crs/misc/R44597.pdf>.
  88. Ibid., 10.

- 
89. Birch Bayh, “Statement of Birch Bayh to the National Institutes of Health,” May 25, 2014, <http://www.essentialinventions.org/drug/nih05252004/birchbayh.pdf>.
  90. Birch Bayh and Bob Dole, “Our Law Helps Patients Get New Drugs Sooner,” *The Washington Post*, April 11, 2002, [https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/?utm\\_term=.ddb6876a380](https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/?utm_term=.ddb6876a380).
  91. *Ibid.*
  92. National Institute of Standards and Technology (NIST), “Return on Investment Initiative: Draft Green Paper” (NIST, December 2018), 30, <https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf>.
  93. *Ibid.*, 30.
  94. Thomas, “March-In Rights Under the Bayh-Dole Act,” 9.
  95. Peter Arno and Michael Davis, “Why Don’t We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Deriving in Whole or in Part from Federally Funded Research,” *Tulane Law Review* Vol. 75, 631 (2001), [https://engagedscholarship.csuohio.edu/cgi/viewcontent.cgi?article=1754&context=fac\\_articles](https://engagedscholarship.csuohio.edu/cgi/viewcontent.cgi?article=1754&context=fac_articles).
  96. *Ibid.*
  97. John H. Rabitschek and Norman J. Latker, “Reasonable Pricing—A New Twist for March-in Rights Under the Bayh-Dole Act” *Santa Clara High Technology Law Journal* Vol. 22, Issue 1 (2005), 162-163, <https://digitalcommons.law.scu.edu/cgi/viewcontent.cgi?article=1399&context=chtlj>.
  98. *Ibid.*, 163.
  99. *Ibid.* Here, the Presidential Memoranda refers to memoranda produced by the Kennedy and Nixon administrations that pertained to government policy related to contractor ownership of inventions.
  100. *Ibid.*
  101. Dr. Dipanjan “DJ” Nag, Antra Gupta, and Alex Turo, “The Evolution of University Technology Transfer: By the Numbers,” *IPWatchdog*, April 7, 2020, <http://www.ipwatchdog.com/2020/04/07/evolution-university-technology-transfer/id=120451/>.
  102. David M. Hart, “The Impact of China’s Production Surge on Innovation in the Global Solar Photovoltaics Industry” (ITIF, October 2020), <https://itif.org/publications/2020/10/05/impact-chinas-production-surge-innovation-global-solar-photovoltaics>.
  103. Sherisse Pham and Matt Rivers, “China is Crushing the U.S. in Renewable Energy,” *CNN Tech*, July 18, 2017, <http://money.cnn.com/2017/07/18/technology/china-us-clean-energy-solar-farm/index.html>; Hart, “The Impact of China’s Production Surge on Innovation in the Global Solar Photovoltaics Industry.”
  104. Stephen Ezell, “Ensuring U.S. Biopharmaceutical Competitiveness” (ITIF, July 2020), <https://itif.org/publications/2020/07/16/ensuring-us-biopharmaceutical-competitiveness>.
  105. National Science Foundation, “Science and Engineering Indicators: 2020,” “Publications Output: U.S. Trends and International Comparisons,” <https://ncses.nsf.gov/pubs/nsb20214/data>.
  106. National Science Foundation, “Science and Engineering Indicators: 2020,” Appendix table S6-6 (accessed June 11, 2020), <https://ncses.nsf.gov/pubs/nsb20205/data>.
  107. Anna Nishino, “The great medicines migration,” *Nikkei Asia*, April 5, 2022, <https://asia.nikkei.com/static/vdata/infographics/chinavaccine-3/>.
  108. “Safeguarding Pharmaceutical Supply Chains in a Global Economy,” Before the U.S. House Committee on Energy and Commerce, Subcommittee on Health, 116th Cong. (October 30, 2019) (statement of Janet

- 
- Woodcock, Director of FDA Center for Drug Evaluation and Research), <https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019>.
109. Jin Zhang, "The PD-1/PD-L1 Race in China," *PharmExec.com*, June 1, 2018, <http://www.pharmexec.com/pd-1pd-l1-race-china>.
  110. Fangning Zhang and Josie Zhou, "What's next for pharma innovation in China?" McKinsey & Company Pharmaceuticals & Medical Products, September 2017, 2, <https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/whats-next-for-pharma-innovation-in-china>. With CAR-T treatment, cell-killing T-cells are removed from the body and engineered to recognize the relevant cancer target. After the edited T-cells (CAR-Ts) are reintroduced to the patient, they multiply and attack the target cancer cells.
  111. Eric Ng, "Why China is going all out to invent new, stronger, cheaper drugs ... it's not all about challenging the West," *South China Morning Post*, October 2018, <https://www.scmp.com/news/china/society/article/2166462/why-china-going-all-out-invent-new-stronger-cheaper-drugs-its-not>.
  112. Zack Whittaker, "Justice Department Accuses Chinese Spies of Hacking Into Dozens of US Tech and Industry Giants," *TechCrunch*, January 2019, <https://techcrunch.com/2018/12/20/us-indictment-tech-hacks-chinese/>; Derek Lowe, "Chinese Pharma Espionage?" *Science Translational Medicine*, December 15, 2011, [https://blogs.sciencemag.org/pipeline/archives/2011/12/15/chinese\\_pharma\\_espionage](https://blogs.sciencemag.org/pipeline/archives/2011/12/15/chinese_pharma_espionage).
  113. Gryphon Scientific and Rhodium Group, "China's Biotechnology Development: The Role of US and Other Foreign Engagement" (report prepared for the U.S.-China Economic and Security Review Commission, February 2019), 104, <https://www.uscc.gov/Research/china%E2%80%99s-biotechnology-development-role-us-and-other-foreign-engagement>.
  114. Daniel C.K. Chow, "Three Major Problems Threatening Multi-National Pharmaceutical Companies Doing Business in China" (working paper, Ohio State Public Law and Legal Theory, 2017), [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3029347](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3029347).
  115. Robert D. Atkinson, "China's Biopharmaceutical Strategy: Challenge or Complement to U.S. Industry Competitiveness?" (ITIF, August 2019), <https://itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-us-industry>.
  116. Joe Kennedy, "The Link Between Drug Prices and Research on the Next Generation of Cures" (ITIF, September 2019), <https://itif.org/publications/2019/09/09/link-between-drug-prices-and-research-next-generation-cures>.
  117. Philipson and Duric, "Issue Brief: The Impact of HR 5376 on Biopharmaceutical Innovation and Patient Health." 3.
  118. Ibid.
  119. Holtz-Eakin, "Testimony on: The Build Back Better Act's Prescription Drug Policies and Their Potential Impacts," 8.
  120. Ray Esquivel and Rich Croghan, "How Pharmaceutical Companies Can Claim the Orphan Drug Tax Credit," Moss Adams, October 18, 2019, <https://www.mossadams.com/articles/2019/october/orphan-drug-pharmaceutical-credit>.
  121. National Organization for Rare Disorders, "Rare Disease Day: Frequently Asked Questions," <https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf>.
  122. Jennifer Huron, "Impact of the Orphan Drug Tax Credit on Treatments for Rare Diseases" (National Organization for Rare Disorders, June 17, 2015), <https://rarediseases.org/odtcwhitepaper/>.
  123. Ibid.

- 
124. U.S. FDA. “Developing Products for Rare Diseases & Conditions,” <http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/default.htm>.
  125. Rohan Narayanan, “NORD Response to New Draft of the Build Back Better Act,” press release, National Organization for Rare Disorders, October 29, 2021, <https://rarediseases.org/nord-response-to-new-draft-of-the-build-back-better-act/>.
  126. Andrew Brownlee and Joran Watson, “The Pharmaceutical Supply Chain, 2013-2020” (Berkeley Research Group, 2022), 3, <https://www.thinkbrg.com/insights/publications/pharmaceutical-supply-chain-2013-2020/>.
  127. Alia Paavola, “Top PBMs by market share,” *Becker Hospital Review*, May 30, 2019, <https://www.beckershospitalreview.com/pharmacy/top-pbms-by-market-share.html>.
  128. Office of Congresswoman Katie Porter, “Killer Profits”; “High Drug Prices & Monopoly,” *Open Markets Institute*, accessed May 10, 2021, <https://www.openmarketsinstitute.org/learn/drug-prices-monopoly>.
  129. Robert D. Atkinson and Stephen Ezell, “Five Fatal Flaws in Rep. Katie Porter’s Indictment of the U.S. Drug Industry,” (ITIF, May 20, 2021), <https://itif.org/publications/2021/05/20/five-fatal-flaws-rep-katie-porters-indictment-us-drug-industry>. Source: United States Census Bureau, 2002 Economic Census Tables (accessed May 11, 2021), <https://www.census.gov/data/tables/2002/econ/census/manufacturing-reports.html>; United States Census Bureau, 2017 Economic Census Tables (accessed May 11, 2021), <https://www.census.gov/data/tables/2017/econ/economic-census/naics-sector-31-33.html>.
  130. Antonio Ciaccia, “New drug pricing report showcases highs, lows, distorted incentives, and brokenness of Medicare Part D,” 46Brooklyn, December 1, 2021, <https://www.46brooklyn.com/news/2021/12/1/wreckfidera-now-streaming>.
  131. Ibid.
  132. Ibid.
  133. Ibid.
  134. Sood, et al., “Do companies in the pharmaceutical supply chain earn excess returns?” 111.
  135. Stephen Ezell, “Testimony Before the House Oversight Committee on Drug Prices, Intellectual Property, and Biomedical Innovation,” (ITIF, May 2019), 14, <https://itif.org/publications/2019/05/16/testimony-house-oversight-committee-drug-prices-intellectual-property-and>.
  136. Massachusetts Institute of Technology (MIT) Center for Biomedical Innovation, “Welcome to MIT NEWDIGS,” <https://newdigs.mit.edu/>.
  137. W. Nicholson Price II, “Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing,” *Boston College Law Review* Vol. 55, Issue 2 (2014): 492, <https://lawdigitalcommons.bc.edu/bclr/vol55/iss2/5/>.
  138. Rick Mullin, “Off the drawing board,” *Chemical and Engineering News*, April 28, 2019, <https://cen.acs.org/pharmaceuticals/Off-drawing-board/97/i17>.
  139. National Science Foundation, “Programs: Directorate for Engineering (ENG),” <https://www.nsf.gov/funding/programs.jsp?org=ENG>.
  140. Mullin, “Off the drawing board.”
  141. PhRMA, “Prescription Medicines: Insulin Costs in Context,” (PhRMA, January 21, 2021), 10, <https://phrma.org/resource-center/Topics/Cost-and-Value/Prescription-Medicines-Insulin-Costs-in-Context>. Citing: IQVIA, “Medicine Spending and Affordability in the United States” (IQVIA, August 2020), <https://www.iqvia.com/insights/the-iqvia-institute/reports/medicine-spending-and-affordability-in-the-us>.
  142. Novo Nordisk, “My\$99Insulin,” <https://www.novocare.com/insulin/my99insulin.html>.
  143. PhRMA, “Prescription Medicines: Insulin Costs in Context,” 10.

- 
144. Stephen Ezell, “Testimony to the Senate Finance Committee on “Prescription Drug Price Inflation” (ITIF, March 2022), <https://itif.org/publications/2022/03/16/testimony-senate-finance-committee-prescription-drug-price-inflation>.
  145. Blake Pelzer and Paul Spitalnic, “Proposed Safe Harbor Regulation,” Center for Medicare and Medicaid Services: Office of the Actuary, (August 2018), <https://aspe.hhs.gov/sites/default/files/private/pdf/260591/OACTProposedSafeHarborRegulationImpacts.pdf>.
  146. Charles E. Grassley and Ron Wyden, “Insulin: Examining the Factors Driving the Rising Cost of a Century Old Drug,” (United States Senate Finance Committee, January 2021), [https://www.finance.senate.gov/imo/media/doc/Grassley-Wyden%20Insulin%20Report%20\(FINAL%201\).pdf](https://www.finance.senate.gov/imo/media/doc/Grassley-Wyden%20Insulin%20Report%20(FINAL%201).pdf).
  147. Adam J. Fein, “Five Top Drugmakers Reveal List vs. Net Price Gaps (Plus: The Trouble With Insulin Prices),” *Drug Channels*, August 11, 2020, <https://www.drugchannels.net/2020/08/five-top-drugmakers-reveal-list-vs-net.html>.
  148. Ibid.
  149. Ibid.
  150. Ibid.
  151. Adam J. Fein, “Drug Channels News Roundup, July 2020: Diabetes Costs, Regeneron’s Copay Support, MA Rethinks Coupons, My Favorite Chart Updated, and ABC’s Steve Collis,” *Drug Channels*, July 29, 2020, <https://www.drugchannels.net/2020/07/drug-channels-news-roundup-july-2020.html>.
  152. Ibid.
  153. BIO, “Response to Federal Trade Commission: Request for Information on Merger Enforcement,” 14.
  154. Ibid.
  155. Karen Van Nuys et al. “Estimation of the Share of Net Expenditures on Insulin Captured by US Manufacturers, Wholesalers, Pharmacy Benefit Managers, Pharmacies, and Health Plans From 2014 to 2018” *Journal of the American Medical Association Health* Vol. 2, Issue 11 (November 2021), <https://jamanetwork.com/journals/jama-health-forum/fullarticle/2785932>.
  156. PhRMA, “Prescription Medicines: Insulin Costs in Context,” 12.
  157. Ibid., 15.
  158. Association of University Technology Managers (AUTM), “AUTM 2018 Licensing Survey” (AUTM, 2018), 3, [https://autm.net/AUTM/media/SurveyReportsPDF/AUTM\\_FY2018\\_US\\_Licensing\\_Survey.pdf](https://autm.net/AUTM/media/SurveyReportsPDF/AUTM_FY2018_US_Licensing_Survey.pdf); AUTM and the Biotechnology Innovation Organization: “The Economic Contribution of University/Nonprofit Inventions in the United States: 1996-2017,” (AUTM and BIO, June 2019), [https://autm.net/AUTM/media/About-Tech-Transfer/Documents/Economic\\_Contribution\\_Report\\_BIO\\_AUTM\\_JUN2019\\_web.pdf](https://autm.net/AUTM/media/About-Tech-Transfer/Documents/Economic_Contribution_Report_BIO_AUTM_JUN2019_web.pdf).
  159. Justin Chakma et al., “Asia’s Ascent—Global Trends in Biomedical R&D Expenditures” *New England Journal of Medicine* 370 No. 1 (January 2014); ER Dorsey et al., “Funding of US Biomedical Research, 2003-2008” *New England Journal of Medicine* 303 (2010): 137-43, <http://www.ncbi.nlm.nih.gov/pubmed/20068207>.
  160. Neil Turner, “What’s gone wrong with the European pharmaceutical industry,” *Thepharmaletter*, April 29, 1999, <https://www.thepharmaletter.com/article/what-s-gone-wrong-with-the-european-pharmaceutical-industry-by-neil-turner>; David Michels and Aimison Jonnard, “Review of Global Competitiveness in the Pharmaceutical Industry” (U.S. International Trade Commission, 1999), 2-3, <https://www.usitc.gov/publications/332/pub3172.pdf>.
  161. John K. Jenkins, M.D., “CDER New Drug Review: 2015 Update” (PowerPoint presentation, U.S. Food and Drug Administration/CMS Summit, Washington, D.C., December 14, 2015),



---

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM477020.pdf>.

162. Jenkins, “CDER New Drug Review,” 23; Ian Lloyd, “Pharma R&D Annual Review 2020 NAS Supplement,” (PharmaIntelligence, April 2020), 3. <https://pharmaintelligence.informa.com/-/media/informa-shop-window/pharma/2020/files/whitepapers/rd-review-2020-nas-supplement-whitepaper.pdf>.
163. European Federation of Pharmaceutical Industries and Associations, “The Research Based Pharmaceutical Industry: A Key Actor for a Healthy Europe” (EFPIA, 2006).
164. Shanker Singham, “Improving U.S. Competitiveness—Eliminating Anti-Market Distortions” (working paper, International Roundtable on Trade and Competition Policy, 2012).
165. Nathalie Moll, “Would the last pharmaceutical investor in Europe please turn the lights out,” European Federation of Pharmaceutical Industries and Associations blog, January 3, 2020, <https://www.efpia.eu/news-events/the-efpia-view/blog-articles/would-the-last-pharmaceutical-investor-in-europe-please-turn-the-lights-out/>.
166. Neil Turner, “European Pricing Squeeze,” *PharmaExec.com*, October 1, 2002, <https://www.pharmexec.com/view/european-pricing-squeeze>.
167. *Ibid.*