Why Punish Pharma for Making Medicine? Preserving Patent Protections and Cutting Consumer Costs

ABSTRACT

The push to lower pharmaceutical drug prices has taken a stronger foothold in legislative and executive actions in recent years. With average prices rising continuously over the past decade, many consumers struggle to pay for the medications they need—insulin being the most often cited example. Accordingly, a variety of solutions have been suggested. Some solutions support reducing barriers for generic drugs to provide competition to the big brands, others push for greater regulation of manufacturers' ability to price their drugs, and some proposals seek greater transparency to promote price negotiations, especially when compared to prices abroad. Most concerningly, however, one proposition involves restricting the patent system and curtailing patent protections offered to pharmaceutical manufacturers. Doing so would decimate pharmaceutical innovation, curbing the development of novel treatments for diseases such as Alzheimer's and cancer. This Note argues that this must not happen—the patent system must be left alone. The United States is the world leader in pharmaceutical innovation, carrying the bulk of associated expenses too, but this is only possible because of the incentives offered through the US patent system. Pharmaceutical companies, operating in capitalist economies, are just like any other business—existing both to help the public and to seek profits. No other incentive system can match that of current patent protections, and without a way to compensate manufacturers for the billions of dollars and years of trials to bring a new medicine to market, innovation will simply halt. It is therefore vital that the patent system be left alone when considering methods to reduce prescription drug prices. However, doing so does not preclude the success of other proposed solutions. Working with pharmaceutical manufacturers to lower front-end development costs may achieve the desired effects, but penalizing these companies and metaphorically clipping their wings will not.

TABLE OF CONTENTS

In the United States, the public and the government collectively spend more on insulin each year than that of the entire gross domestic product (GDP) of countries such as Jamaica and Nicaragua.[1] Diabetes is the most expensive chronic illness in the United States, with nearly $327 billion spent yearly on treatment and complications.[2] With an average manufacturer price of insulin per standard unit in the United States of $98.70,[3] some diabetics face out-of-pocket costs reaching $1,000 per month, depending on insulin type and insurance coverage.[4] For many of the estimated six million Americans that require daily insulin to manage their diabetes, the price of the drug is too high, especially without adequate insurance—to the extent that nearly one

1. An average of $15 billion is spent on insulin in the United States each year. Erin M. Barker, *When Market Forces Fail: The Case for Federal Regulation of Insulin Prices*, 42 CAMPBELL L. REV. 311, 315 (2020); *GDP (current US$)*, THE WORLD BANK, https://data.worldbank.org/indicator/Ny.Gdp.Mktp.Cd [perma.cc/EWX9-GENY] (last visited Jan. 29, 2021).

2. Barker, *supra* note 1.

3. ANDREW W. MULCAHY, DANIEL SCHWAM & NATHANIEL EDENFIELD, COMPARING INSULIN PRICES IN THE UNITED STATES TO OTHER COUNTRIES: RESULTS FROM A PRICE INDEX ANALYSIS 10 (RAND Corp. 2020), available at https://www.rand.org/pubs/research_reports/RRA788-1.html [perma.cc/4KZ4-5JBU] [hereinafter RAND].

4. Barker, *supra* note 1, at 312.

in four ration insulin to keep expenses down.[5] Issues with prescription drug prices in the United States extend beyond diabetes and insulin. One study suggests that 25 percent of Americans struggle to pay out-of-pocket costs for prescription drugs.[6] Even the federal government has seen a 76 percent increase in spending on prescription drugs since 2000, at numbers now exceeding $457 billion annually for Medicare and Medicaid.[7] Quite clearly, an issue exists that must be addressed; the country with the most advanced health care system in the world has one in four citizens struggling to afford their medications.[8] Perhaps the need to address exorbitant prescription drug prices in the United States is better framed in this context: costs of prescriptions drugs in the United States are 256 percent higher than the average of all other member countries of the Organisation for Economic Co-Operation and Development (OECD).[9] However, attempts to resolve this predicament cannot, and should not, impact the patent system and its protection of pharmaceutical innovations.

I. THE PROGRESSION OF THE PHARMACEUTICAL DRUG PRICE PREDICAMENT

Contextualizing the inordinate drug prices in the United States, especially in comparison to prices around the rest of the world, requires contemplation of the greater context and history of the pharmaceutical industry and the uniqueness of pharmaceuticals in the United States. Consider insulin. The original patent for insulin was granted to Frederick Banting, Charles Best, and J.B. Collip in 1923.[10] Under agreement with the University of Toronto, to whom the patent ownership had been previously sold, Eli Lilly was subsequently granted

5. Jeremy A. Greene & Kevin R. Riggs, *Why is There No Generic Insulin? Historical Origins of a Modern Problem*, 372 NEW ENG. J. MED. 1171, 1171 (2015); *see also* Barker, *supra* note 1, at 316 (estimating 7.4 million people require daily insulin).

6. S. Vincent Rajkumar, *The High Cost of Prescription Drugs: Causes and Solutions*, 10 BLOOD CANCER J., 1, 1 n.3 (2020) (citing the KFF Health Tracking Poll, conducted February 2019 and displayed on the Peterson-KFF Health System Tracker).

7. ANDREW W. MULCAHY, CHRISTOPHER M. WHALEY, MAHLET GIZAW, DANIEL SCHWAM, NATHANIEL EDENFIELD & ALEJANDRO URIEL BECERRA-ORNELAS, INTERNATIONAL PRESCRIPTION DRUG PRICE COMPARISONS: CURRENT EMPIRICAL ESTIMATES AND COMPARISONS WITH PREVIOUS STUDIES 1 (RAND Corp. 2021), available at https://www.rand.org/pubs/research_reports/RR2956.html [perma.cc/HVW8-GDMD].

8. Rajkumar, *supra* note 6.

9. MULCAHY ET AL., *supra* note 7, at vii, xv.

10. Louis Rosenfeld, *Insulin: Discovery and Controversy*, 48 CLINICAL CHEMISTRY 2270, 2280 (2002).

a license to the patent for drug improvements.[11] After the original patent expired, numerous improvements were made to insulin throughout the twentieth century by various actors, mainly Eli Lilly, Novo Nordisk, and Sanofi, the three primary insulin manufacturers today.[12] Each of these subsequent improvements were properly afforded patent protection, and a market monopoly rightly ensued for each specific form of insulin created, beginning with Nordisk's development of crystalline protamine-isophane insulin for prolonged action in 1946.[13] At this time, however, insulin was sourced from beef and pork and was thus filled with impurities.[14] To address such impurities, Eli Lilly developed single peak insulins in the 1970s and made the first recombinant insulin to human insulin; Nordisk later made monocomponent insulins for improved safety.[15] Numerous improvements and modifications to insulin were further made over the next two decades for greater safety and efficacy.[16] Each of these new versions were awarded patent protection, granting each manufacturer a temporary monopoly of the market for roughly twenty years: an incentive that awards complete freedom of pricing and a reward explicitly granted by the Constitution.[17] However, many are still dissatisfied with the cost of insulin nearly a century later, and even more so because insulin costs ten times more in the United States than

11. The University of Toronto was sold the original US insulin patent for one dollar. Upon realizing they did not have the expertise or market foothold to improve and sell better versions of insulin, the University teamed up with Eli Lilly. Lilly was permitted to apply for further patents for any improvements, while the University retained the rights to patent rights for the rest of the world. The University also licensed the rights to other companies such as Nordisk in Denmark. Greene & Riggs, *supra* note 5, at 1171–72.

12. Barker, *supra* note 1, at 318.

13. A decade later, Nordisk then introduced "slow" insulin that prolonged the action of insulin without the addition of protamine, as required in their earlier patented versions. Greene & Riggs, *supra* note 5, at 1172.

14. Insulin from animal pancreases have similar pharmacokinetics and pharmacodynamics; however, the formation of anti-insulin antibodies was common and led to insulin resistance in patients. Irl B. Hirsch, Rattan Juneja, John M. Beals, Caryl J. Antalis & Eugene E. Wright, Jr., *The Evolution of Insulin and How It Informs Therapy and Treatment Choices*, 41 ENDOCRINE REV. 733, 735 (2020).

15. Single peak insulin, also known as monocomponent insulin, is a form of insulin that has been purified into only active insulins through chromatographic processing techniques, created to avoid the buildup of anti-insulin antibodies in patients. *Id.* at 735–736.

16. *See id.*

17. John H. Barton & Ezekiel J. Emanuel, *The Patents-Based Pharmaceutical Development Process*, 294 J. AM. MED. ASS'N 2075, 2076 (2005) (citing U.S. CONST. art. I, § 8, cl. 8) (Congress has the power "[t]o promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive rights to their respective writings and discoveries").

in all other OECD countries.[18] The outcry to reduce prescription drug prices, with frequent references to insulin as a case in point, has existed for many years but has rapidly gained further traction within the past two years.[19]

Today, pushback against pharmaceutical drug prices has increasingly caught the attention of the federal government, as seen in recent efforts by the White House and Congress. Prior to the end of his time in office, former President Trump issued three executive orders addressing drug prices and acknowledging the disproportionately high cost as compared to prices abroad.[20] Trump's first executive order sought to increase importation of prescription drugs from other countries where prices are lower, reducing trade barriers to increase competition.[21] The second and third sought to impose most-favored-nation[22] prices on government purchases for Medicare, thus entitling the United States to the best price for a drug currently offered to any other country.[23] President Biden also issued an order on similar grounds, instructing the Secretary of Health and Human Services to lower prices of prescription drugs.[24] In 2021 alone, no fewer than seven bills were introduced in Congress seeking to address the problem.[25] Several focus mostly on price negotiations and most-favored-nation pricing strictly for Medicare and government programs,[26] while others look to solve the drug pricing issue through other measures such as promoting biosimilars and generics, increasing

---

18. MULCAHY ET AL., *supra* note 3, at 16.

19. *See* Joseph Choi, *Advocates Press Congress to Address High Insulin Costs*, HILL (Nov. 14, 2022, 2:03 PM), https://thehill.com/policy/healthcare/3734438-advocates-press-congress-to-address-high-insulin-costs/ [perma.cc/6RJU-W6UF].

20. *See* Exec. Order No. 13,938, 85 Fed. Reg. 45,757 (July 29, 2020); Exec. Order No. 13,947, 85 Fed. Reg. 59,171 (Sept. 18, 2020); Exec. Order No. 13,948, 85 Fed. Reg. 59,649 (Sept. 23, 2020).

21. Exec. Order No. 13,938, 85 Fed. Reg. at 45,757.

22. Most-favored-nation status is a principle in which state treats all of its trading partners equally, such that the most favorable terms offered to one state must also be offered to all other states. *Most Favored Nation*, CORNELL L. SCH: LEGAL INFO. INST., law.cornell.edu/wex/most_favored_nation [perma.cc/KJ7R-EP4U] (last visited Sep. 24, 2022).

23. Exec. Order No. 13,947, 85 Fed. Reg. at 59,171 (citing that other countries enjoy bargain prices because the United States finances most biopharmaceutical innovation, both privately and publicly); Exec. Order No. 13,948, 85 Fed. Reg. at 59649.

24. Exec. Order No. 14,036, 86 Fed. Reg. 36,987 (July 14, 2021) ("It is also the policy of my Administration to support aggressive legislative reforms that would lower prescription drug prices.").

25. *See* H.R. 2071, 117th Cong. (2021); H.R. 2148, 117th Cong. (2021); H.R. 3, 117th Cong. (2021); H.R. 2181, 117th Cong. (2021); S. 898, 117th Cong. (2021); H.R. 2884, 117th Cong. (2021); S. 909, 117th Cong. (2021).

26. H.R. 3; *see also* H.R. 2181; S. 898.

federal price regulation, and amending patent laws to restrict pharmaceutical companies.[27]

The issue of drug pricing has wandered into US courts as well. For example, drug manufacturer AbbVie Inc. found itself subject to a class action suit in 2020 based on antitrust concerns and anticompetitive behavior with its arthritis and immunosuppressive drug, *Humira*.[28] However, the courts are an unlikely avenue for successful pushback against high pharmaceutical drug prices, as the US District Court for the Northern District of Illinois found that "AbbVie has exploited advantages conferred on it through lawful practices [including the patent system] and to the extent this has kept prices high for Humira, existing antitrust doctrine does not prohibit it."[29] While the Supreme Court recently ruled for the benefit of consumers by permitting states to implement laws that regulate pharmacies' ability to set prices for prescriptions paid for by employee health plans, this recent decision does not implicate drug manufacturers and the initial prices they set, but rather price setting down the consumer chain.[30] Because freedom of price setting and market exclusivity are incontestably permitted by the Constitution, the courts have their metaphorical hands tied and are of little use in attempts to reduce prescription drug prices.[31]

The prices of many pharmaceutical drugs in the United States are justly a cause for concern, especially given the contrast in pricing with the rest of the world.[32] During the first six months of 2019 alone, prescription drug prices in the United States rose over five times the rate of inflation.[33] Accordingly, it is no surprise that the federal government has initiated a variety of recent actions to address the situation.[34] However, for reasons addressed below, solutions to the high pharmaceutical drug prices in the United States should not impose limitations on the current patent system nor reduce the protections and incentives that patents currently offer pharmaceutical companies.

---

27. H.R. 2884; S. 909.

28. *See In re* Humira (Adalimumab) Antirust Litigation, 465 F. Supp. 3d 811, 819, 825 (2020).

29. *Id.* at 819.

30. *See* Rutledge v. Pharm. Care Mgmt. Ass'n, 141 S. Ct. 474, 478 (2020).

31. *See* U.S. CONST. art. I, § 8, cl. 8.

32. *See* MULCAHY ET AL., *supra* note 3, at 12.

33. Kathleen Iacocca & Beth Vallen, *Using Analytics to Gain Insights on U.S. Prescription Drug Prices: An Inductive Analysis*, 40 J. PUB. POL'Y & MKTG. 538, 538 (2021). The average price for 3,400 prescription drugs increased 10.5 percent from January to June of 2019. *Id.*

34. *See supra* notes 21, 23–27.

II. THE CURRENT CIRCUMSTANCES CONTRIBUTING TO COSTS

Determining the appropriate price for a new drug is one of the most difficult challenges faced by pharmaceutical manufacturers because of the many factors that must be taken into account.[35] Manufacturers must consider the cost-effectiveness of each drug, research and development (R&D) costs, and the price of existing therapies and competing products, among an array of other factors, each of which varies from product to product.[36] Critics of "Big Pharma" also forget to consider that most pharmaceutical manufacturers in the United States are for-profit companies existing in a capitalist economy, so logically such companies incorporate some degree of a profit margin as well.[37] Contrary to what some may think or believe, seeking to profit from the development of innovative products is constitutionally permissible; the entire purpose of the patent system is to encourage innovation by rewarding inventors.[38] Patent protection, which provides twenty years of market exclusivity and permits manufacturers to price their patented products as they wish, allows pharmaceutical investment to be profitable and exceed the costs of capital.[39] Pharmaceutical manufacturers cite high prices as the fuel for further innovation,[40] and this is a reality—revenue from drug pricing is how companies cover the costs of finding new cures and developing new drugs. Nothing is ever free.

This innovation, measured predominantly through R&D, requires significant investment.[41] The Congressional Budget Office (CBO) estimates that 25 percent of pharmaceutical revenue is reinvested into R&D;[42] other sources suggest numbers around 17

35. P. Roy Vagelos, *Are Prescription Drug Prices High?*, 252 SCIENCE 1080, 1081 (1991).

36. *Id.* ("[I]t is important to establish prices for our products that will produce an appropriate return on our research investment and maximize patient access. If the price is too high and the patient cannot afford the medicine, we have not fulfilled our reason for existence.").

37. Iacocca & Vallen, *supra* note 33, at 539.

38. Barton & Emanuel, *supra* note 17.

39. *See* Tahir Amin, *Patent Abuse is Driving Up Drug Prices. Just Look at Lantus*, STAT (Dec. 7, 2018), https://www.statnews.com/2018/12/07/patent-abuse-rising-drug-prices-lantus/ [perma.cc/P7U5-6VTH]. *But see* Vagelos, *supra* note 35, at 1082. In reality, however, despite the intent for patent protection to allow manufacturers to profit from their inventions, very few drugs actually manage to recoup their investment costs. *Id.*

40. Rajkumar, *supra* note 6.

41. Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 20 (2016).

42. CONG. BUDGET OFF., RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY 1 (Apr. 2021) [hereinafter CBO].

percent.[43] Investment into R&D is based on factors such as anticipated lifetime global revenues of a particular drug, expected development costs, and government policies influencing its supply and demand.[44] Despite drug prices increasing five times the rate of inflation during the first six months of 2019,[45] the pharmaceutical industry devoted $83 billion to R&D that year, more than ten times the annual expenditures during the 1980s.[46] The Food and Drug Administration (FDA) is also now approving around 60 percent more drugs annually than during the previous decade.[47] Clearly, even though drug prices are rapidly rising, so are both the amount of investment and the demand for development of new medicine.[48]

The increase in prescription drug prices nowadays is dwarfed, however, by the modern-day cost of developing new medicines. As pharmaceutical manufacturers aim to tackle even more complex diseases, and as the complexity of pharmaceutical innovation increases accordingly, the costs of developing a single new drug today are estimated to surpass $3 billion.[49] Other estimates quote novel drug production at even higher prices, especially considering development averages about twelve years from start to finish.[50] Even after these mass expenditures of time and money, and on the further contingency that a drug even passes clinical trials, the FDA still ultimately approves only 21 percent of new drugs presented for its consideration.[51] Price increases, conventionally associated with higher R&D costs, can also be attributed to the nature of the world's pharmaceutical landscape. The United States' infrastructure is used internationally for preclinical and clinical trials, and subsequently the US market absorbs a large chunk of international R&D costs.[52] The increase in drug prices observed in

43. G. Caleb Alexander, Jeromie Ballreich, Mariana P. Socal, Taruja Karmarkar, Antonio Trujillo, Jeremy Greene, Joshua Sharfstein & Gerard Anderson, *Reducing Branded Prescription Drug Prices: A Review of Policy Options*, 37 PHARMACOTHERAPY 1469, 1471 (2017).

44. CBO, *supra* note 42.

45. Iacocca & Vallen, *supra* note 33.

46. CBO, *supra* note 42.

47. *Id.*

48. *Id.*

49. Rajkumar, *supra* note 6, at 1–2. The estimated cost of developing a new medicine takes into account failure rates and sunken costs on failed versions. *Id.* at 2.

50. Vagelos, *supra* note 35, at 1080; Michael Schlander, Karla Hernandez-Villafuerte, Chih-Yuan Cheng, Jorge Mestre-Ferrandiz & Michael Baumann, *How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment*, 39 PHARMACOECONOMICS 1243, 1246 (2021).

51. CBO, *supra* note 42, at 2; *see also* Barton & Emanuel, *supra* note 17 (showing that only 21 percent of drugs that begin human testing are actually approved).

52. Laura Bailey, *Why are U.S. Drug Prices so High? What Should a Presidential Policy to Lower Drug Costs Include?*, MICH. NEWS (Oct. 29, 2020), https://news.umich.edu/why-are-us-

the United States is therefore not entirely by choice of manufacturers, but rather a consequence of the need for complex innovation, market demand, and a reliance of foreign companies on the US pharmaceutical industry.

To add further difficulty in pricing new drugs, prescription drugs do not exist under normally functioning economic environments.[53] Not only can prices be set above expected competitive market price under patent protections, but surprisingly, when new competitors do enter the market, there have been instances of existing drugs subsequently increasing in price.[54] Pharmaceutical companies also initially market their drugs in a market that is largely unregulated when it comes to price,[55] yet operate in a market that is subject to substantial government influence.[56] On one hand, the federal government increases demand by subsidizing the purchase of prescription drugs through programs such as Medicare and Medicaid; on the other, the government increases supply by funding private industry.[57] Public-sector pharmaceutical research increases the prices of private firm research too, acting not as a substitute to private R&D but rather as a compliment.[58] In the pharmaceutical industry, therefore, the government is both largely involved yet simultaneously uninvolved,[59] which only serves to complexify the market. The dichotomy of government influence over supply and demand and its deregulation of price, the balance between profit and access, and the atypical results of competition all serve to further convolute the drug pricing process for manufacturers.

In addition to ever-growing R&D costs, many argue that the most significant reason for high drug prices is the monopoly granted

---

drug-prices-so-high-what-should-a-presidential-policy-to-lower-drug-costs-include/ [perma.cc/5BZR-BMCW]. According to the World Health Organization, between 1999 and 2021, the United States was the location of 132,952 interventional clinical trials, compared to the 54,499 trials in China, the second most common location for such trials. *See Number of Clinical Trial Registrations by Location, Disease, Phase of Development, Age and Sex of Trial Participants (1999–2021)*, WORLD HEALTH ORG. (Feb. 2022), https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/number-of-trial-registrations-by-year-location-disease-and-phase-of-development [perma.cc/QX4R-TKZ3] [hereinafter WHO].

53. Alexander et al., *supra* note 43, at 1471–72 (indicating that evidence suggests that drug pricing doesn't conform to standard economic models).

54. *Id.* at 1472.

55. John A. Vernon, *Examining the Link Between Price Regulation and Pharmaceutical R&D Investment*, 14 HEALTH ECONS. 1, 1 (2005); *see also* CBO, *supra* note 42, at 23 (stating that US markets are subject to less price regulation than abroad).

56. CBO, *supra* note 42, at 2.

57. *Id.*

58. *Id.*

59. *See supra* note 57 and accompanying text.

through the patent system.[60] Basic economic theory holds that "firms will undertake the most profitable investment projects first . . . and continue to [do so as] long as the expected rate of return . . . exceeds the firm's marginal cost of capital."[61] The patent system allows pharmaceutical companies to achieve just that. The patent protection window includes time to develop and fine-tune medicines further, while delaying FDA approval of generics and biosimilars.[62] Given the abnormal market conditions under which pharmaceutical companies operate, patent protection is often extended due to the recognition that drugs cannot be sold until after clinical trials have been completed, even though patent protection must be granted before these trials take place.[63] The 1984 Hatch-Waxman Act therefore grants upwards of five additional years of protection to make up for time lost during clinical trials.[64] Other extensions of patent protection include an additional seven years under the Orphan Drug Act of 1983 for drugs that treat conditions with fewer than 200,000 instances or for drugs where market conditions make recovering R&D costs impossible.[65]

When these patent protections expire, generic manufacturers are then permitted, without legal repercussions, to produce and sell formerly patented drugs with hopes that competition may reduce the price of a particular treatment on the market.[66] However, as mentioned above, the pharmaceutical market does not always mirror typical economic trends—as exemplified by instances where patent expiration has not resulted in lower pricing—thus opening the door for further criticism of the patent system.[67]

III. COMMONLY SUGGESTED SOLUTIONS TO THE SITUATION

A. Generics and Biosimilars

One common proposal for reducing prescription drug prices is through the further development of generic and biosimilar options to formerly patented drugs, as promoted in President Biden's recent

60. *See* Amin, *supra* note 39; *see also* Rajkumar, *supra* note 6.
61. Vernon, *supra* note 55, at 2.
62. *See* CBO, *supra* note 42, at 2.
63. *Id.* at 21.
64. *Id.*; Barton & Emanuel, *supra* note 17.
65. CBO, *supra* note 42, at 21.
66. *See* Rajkumar, *supra* note 6, at 1–2.
67. *See* Iacocca & Vallen, *supra* note 33, at 541–42.

executive order.[68] The intention here is to promote the development of off-patent medicines that compete in the marketplace with the brand-name originals and effectively lower prices through typical mechanics of marketplace competition.[69] Generic medicines are bioequivalents, meaning that the active ingredients are identical to the original drug, and typically exist for small, less complicated drugs that are easy to synthesize.[70] Alternatively, biosimilars are a relatively new creation and serve to replicate large-molecule, biologic drugs (those synthesized from living organisms).[71] With biosimilars however, the new "off-patent" version are rarely identical to the original—it instead looks to mimic the effects of the original drug by targeting the same therapeutic goal with similar mechanics.[72]

Advocates for further development of generics and biosimilars often call for faster approval by simplifying the regulatory process of these drugs beyond the legislation already in place to get generics and biosimilars to the market quicker.[73] However, such efforts may not yield the desired results. Bringing generics and biosimilars to the market after patent expiry of the original drugs would, under typical macroeconomic theories, reduce the price of a given drug by increasing supply and creating competition.[74] As indicated previously, however, pharmaceuticals do not always follow typical market trends.[75] One study shows that while generics provide lower-cost alternatives to brand-name drugs, the downward pressure on prices is often felt by other generic competitors rather than the original manufacturer.[76] In

68. *See* Exec. Order 14,036, *supra* note 24, at 36,997. Biden's Order aims "to lower the prices of and improve access to prescription drugs and biologics, continue to promote generic drug and biosimilar competition . . . by (A) continuing to clarify and improve the approval framework for generic drugs and biosimilars to make generic drug and biosimilar approval more transparent, efficient, and predictable." *Id.*

69. *See* Katelijne van de Vooren, Alessandro Curto & Livio Garattini, *Biosimilar Versus Generic Drugs: Same But Different?*, 13 APPLIED HEALTH ECON. HEALTH POL'Y 125, 125 (2015).

70. *Id.*

71. *See* CBO, *supra* note 42, at 21–22.

72. *Id.* at 22. Title VII of the Patient Protection and Affordable Care Act (PPACA) aims to balance innovation and consumer interests when creating such a biosimilar pathway. *See* Consolidated Appropriations Act of 2023, Pub. L. No. 117-328, 136 Stat. 4459 (2022).

73. *See* Rajkumar, *supra* note 6, at 2. The Hatch-Waxman Act permits generics to be approved without clinical trials, while the PPACA created an abbreviated pathway for the approval of biosimilars. The PPACA also encourages the development of generics by protecting manufacturers from claims of patent infringement when trying to develop generics before the original patents have expired. CBO, *supra* note 42, at 21.

74. Iacocca & Vallen, *supra* note 33, at 540.

75. *Id.*

76. *Id.* at 541; *see also* Ernst R. Berndt, Richard Mortimer, Ashoke Bhattacharjya, Andrew Parece & Edward Tuttle, *Authorized Generic Drugs, Price Competition, and Consumers' Welfare*, 26 HEALTH AFFS. 790, 797–98 (2007) (finding that additional generic competition places a

fact, there have also been instances where the price of brand-name drugs actually increases when a generic version entered the market.[77] Furthermore, the presence of a generic drug does not always mean that a lower-cost alternative exists; in drug classes related to heart rhythms, depression, and genitourinary issues, the average price of a generic drug has actually been found to be higher than the original.[78] Consider Novartis' leukemia treatment, *Gleevec*, for example, which was introduced to the market in 2001 at a list price of $26,000; biosimilar drugs that now compete with Gleevec run at prices around $150,000.[79] Traditional mechanisms of competition to reduce prices, i.e., the introduction of generics and biosimilars to the market, are therefore seemingly either inconsistent, ineffective, or both in the pharmaceutical consumer industry.[80]

Insulin is a particularly complicated example of such ineffectiveness. By the start of 2016, eleven of the most commonly sold insulin products in the United States were no longer under patent protection,[81] suggesting that the competitive market should, in theory, be wide open and prices should subsequently drop. However, vocal advocates for further development of generics and biosimilars, particularly for treating diabetes, face significant obstacles. Firstly, off-patent insulin can only be produced as a biosimilar given its large molecular size.[82] Off-brand replicas of insulin are therefore not identical on an atom-by-atom basis, but instead target the same therapeutic goal—allowing cells to absorb glucose from the blood.[83] These minor differences can result in inconsistencies in protein folding and other processes that affect efficacy and safety; FDA approval of biosimilars therefore requires much more regulation and safety, which in turn

downward pressure on overall generic prices and that "additional generic entrants after the first four or five do not appear to significantly affect long-run generic-to-brand price ratios").

77. Iacocca & Vallen, *supra* note 33, at 541 (citing Kathleen Iacocca, James Sawhill & Yao Zhao, *A Multiple Regression Model to Explain the Cost of Brand-Drugs*, 47 SOCIO-ECONOMIC PLAN. SCIS. 238, 239 (2013)).

78. *Id.* at 545.

79. Iacocca & Vallen, *supra* note 33, at 542.

80. *See* CBO, *supra* note 42, at 16–17, 23–24; *see also* Iacocca & Vallen, *supra* note 33, at 542.

81. Jing Luo & Aaron S. Kesselheim, *Evolution of Insulin Patents and Market Exclusivities in the USA*, 3 LANCET DIABETES & ENDOCRINOLOGY 835, 837 (2015).

82. Greene & Riggs, *supra* note 5, at 1173. Insulin is a large-molecule biologic drug (coming from living organisms) that is not a single entity but rather a family of related products. Such complex biologics are much more challenging to copy in the generic drug industry. *Id.*

83. *Id.*; *Biosimilar Insulin Treatment: What the Science Says*, ENDOCRINE SOC'Y (Sept. 28, 2022), https://www.endocrine.org/patient-engagement/hormone-headlines-blog/biosimilar-insulin-treatment [perma.cc/XSV5-6SAB].

minimizes possible price reductions.[84] One study found that because biosimilars are subject to extensive regulation, the resulting price discount was 40 percent from the price of the original drug at most, whereas generics, which are subject to substantially less regulation, can see upwards of 80 percent cost discounts.[85] So far, the FDA has approved two biosimilar insulins, *Basaglar* and *Admelog*, in 2015 and 2017 respectively, yet complaints about the price of insulin continue.[86] Manufacturers of generics and biosimilars, such as those mentioned above, struggle with incentivization too. It is true that as modifications to existing brand-name drugs are made and granted patent protection, "doctors are still quite able to prescribe the generic versions of the older product" if they exist.[87] However, as new and improved versions come to market, most generic drug companies have evidently not considered it worthwhile to invest in creating biosimilar versions of insulin that are now obsolete, less effective, or below the standard of care.[88] If there is not enough money or demand in the market for older versions of insulin, companies will not choose to invest in developing biosimilar equivalents once patents expire.[89]

B. Greater Transparency

Another commonly proposed solution to high prescription drug prices is for greater transparency between manufacturers and consumers.[90] Not that transparency itself necessarily leads to lower drug costs, but rather it would in theory permit price negotiations and the ability to hold manufacturers accountable to reasonable pricing schemes.[91] Twenty-two states have already passed legislation requiring

84. Greene & Riggs, *supra* note 5, at 1173.

85. *Id.* Noninsulin biosimilars approved in Europe have also seen disappointingly small price reductions compared to the original versions, with economists warning that "the introduction of biosimilars may not lead to price reductions equivalent to those seen with typical generic medicines." *Id.*

86. Jentora White, Afton Wagner & Hima Patel, *The Impact of Biosimilar Insulins on the Diabetes Landscape*, 28 J. MANAGED CARE & SPECIALTY PHARMACY 91, 91–92 tbl.1 (2022). The FDA also recently approved the first interchangeable biosimilar insulin, Semglee, in 2021, but questions still exist whether the cost of insulin will decrease by more than 20 percent, as seen with other biosimilars. *Id.*; Greene & Riggs, *supra* note 5, at 1173.

87. Roger Collier, *Drug Patents: The Evergreening Problem*, 185(9) CANADIAN MED. ASS'N J. E385, E385 (2013).

88. *See* Greene & Riggs, *supra* note 5, at 1173; *see also* Rajkumar, *supra* note 6, at 1, 3.

89. *See* Rajkumar, *supra* note 6. The issue of demand in the market is exacerbated by consumer tendencies to gravitate towards the reputability of brand-name products. *See* Iacocca & Vallen, *supra* note 33, at 551; CBO, *supra* note 42.

90. *See* Bailey, *supra* note 52.

91. Iacocca & Vallen, *supra* note 33, at 553.

reporting by manufacturers for annual price increases or when drugs have estimated annual costs exceeding a certain amount, all with hopes of understanding the factors that lead to drug pricing.[92] These reporting requirements placed on manufacturers may be a double-edged sword, though; while they may empower pharmacies and consumers to negotiate for lower prices, manufacturers allege that imposing additional administrative costs only risks increasing consumer costs.[93] In fact, one of the greatest criticisms of greater transparency requirements is that the unreasonable administrative burden substantially outweighs the benefits it may confer.[94]

The true impact of greater transparency is still mostly guesswork. A 2016 study noted that the prices paid for a given medical device by some hospitals varied considerably, but when given access to a common database of prices paid by other medical facilities, hospitals were able to negotiate lower prices.[95] America's Health Insurance Plans, a national political advocacy group of health insurance providers, hopes that a similar effect could occur on prescription drug prices as seen in the above 2016 study.[96] The group attests that "drug transparency laws will improve the bargaining ability that state health agencies, pharmacy benefit managers, and health insurance providers have when negotiating drug prices with drug makers and will consequently lead to lower prices."[97] However, the potential to negotiate lower prices will not lead manufacturers to ignore overhead costs and R&D expenses, the main influences behind pricing policy.[98] Very few prescription drugs actually recoup the cost of their development in the first place, and manufacturers subsequently take a loss, so the thought that drug manufacturers would be willing to accept even greater losses if prices are negotiated lower is unfathomable.[99]

Perhaps the need for transparency is better targeted toward other actors.[100] Pharmaceutical drugs are commonly sold indirectly to consumers, and therefore products pass through a complex supply

92. AHIP, WHY PRESCRIPTION DRUG PRICE TRANSPARENCY MATTERS 3 (June 2018), https://www.ahip.org/documents/AHIP_IssueBrief_RxTransparency_62018FINAL.pdf [perma.cc/8MKZ-6P36].

93. Iacocca & Vallen, *supra* note 33, at 538–39.

94. AHIP, *supra* note 92, at 2.

95. *Id.* at 10.

96. *Id.*

97. *Id.*

98. *See* Chaarushena Deb & Gregory Curfman, *Relentless Prescription Drug Price Increases*, 323 J. AM. MED. ASS'N 826, 826 (2020).

99. Vagelos, *supra* note 35, at 1082; *see* CBO, *supra* note 42.

100. *See* Rajkumar, *supra* note 6, at 4.

chain, more so than other consumer goods.[101] Prescription drugs are sold to wholesale distributors who supply retailers such as pharmacies and hospitals, who can then only deal with physicians acting as agents of consumers.[102] Pharmacy benefit managers (PBMs) and health insurance providers further complicate the supply chain, and thus imposing transparency requirements on the manufacturers only reveals part of the picture.[103] Transparency arrangements between middlemen may be more effective, for example, to ensure that rebates secured by PBMs from the manufacturers are passed to consumers as savings, rather than kept as profits.[104] Therefore, while increasing transparency requirements on manufacturers may hold such companies accountable or encourage price negotiations, the pharmaceutical industry and supply chains may be too complex to reduce prices for consumers predictably with this method.[105]

C. Government Regulation and Price Caps

A variety of bills seeking greater government involvement in pricing prescription drugs and calling for price caps or the implementation of penalties for price increases have circulated—or are currently circulating—through Congress.[106] Most countries around the world have some form of government regulation of prescription drug prices;[107] however, imposing similar constraints on US pharmaceuticals threatens the proliferation and success of these companies as world leaders.[108] Some federal agencies already purchase drugs at prices subject to a statutory cap or with the benefit of statutory rebates,[109] but additional price regulations are almost guaranteed to stifle innovation.[110] Pharmaceutical price regulation exerts negative pressure

101. Iacocca & Vallen, *supra* note 33, at 539.

102. *Id.*

103. *Id.* PBMs are "third party companies that function as intermediaries between insurance providers and pharmaceutical manufacturers. PBMs create formularies, negotiate with manufacturers, process claims, create pharmacy networks, review drug utilization, and occasionally manage mail-order specialty pharmacies." *Pharmacy Benefit Managers*, NAT'L ASS'N OF INS. COMM'RS, https://content.naic.org/cipr-topics/pharmacy-benefit-managers [perma.cc/6M8S-YGDH] (Apr. 11, 2022).

104. Rajkumar, *supra* note 6, at 4.

105. Iacocca & Vallen, *supra* note 33, at 554 ("Collaboration with members of the supply chain in this way may help realign incentives but it is important to note that the complexities of pricing in this industry argue against most 'one-size fits all' strategies.").

106. *See* Deb & Curfman, *supra* note 98, at 826.

107. *See* CBO, *supra* note 42.

108. Vagelos, *supra* note 35, at 1080.

109. CBO, *supra* note 42, at 23.

110. *See* Bailey, *supra* note 52.

on a company's expected returns on its R&D investment—a risk that may outweigh its reward if imposed on US pharmaceutical companies.[111] In fact, one analysis showed that limiting profit margins of US pharmaceutical companies to levels of non-US manufacturers in countries where price regulation exists would decrease R&D intensity upwards of 30 percent.[112]

The imposition of price controls on private sector pharmaceutical development would massively limit the rate of pharmaceutical innovation, commonly proxied with R&D expenditure.[113] One estimation based on existing literature suggests a 29.2 to 60 percent reduction in R&D over the next twenty years resulting from the price controls suggested by President Biden.[114] In order to estimate a return on investment for any given R&D project, pharmaceutical manufacturers predict the market landscape and estimated profits; literature suggests a positive relationship between realized revenues, R&D spending, and innovation.[115] Predictions of global revenues drive R&D investment; however, manufacturers currently enjoy 64 to 78 percent of their global profits from the United States alone.[116] Price regulation limiting these expected profits in the United States will dramatically reduce R&D expenditures based on the observed positive relationship between the two factors.[117]

The CBO estimates that imposing President Biden's price control measures would only lead to eight fewer drugs produced over the next decade,[118] but this finding is miscalculated because the CBO reported the lower extreme of its estimates and used small markets as the basis for such estimates.[119] University of Chicago Professor Tomas Philipson and his colleague Troy Durie[120] recently reworked the CBO's

111. Vernon, *supra* note 55, at 2–3.

112. *Id.* at 11–12.

113. Tomas Philipson & Troy Durie, *The Evidence Base on the Impact of Price Controls on Medical Innovation* 4 (Becker Friedman Inst. For Econ. at Univ. of Chicago, Working Paper No. 2021-108, 2021).

114. *Id.* Measured in units other than percentage decrease, this equates to lost spending between $952.2 billion to $2 trillion, or 167 to 342 fewer drug approvals between 2021 and 2039. *Id.*

115. *Id.* at 2.

116. *Id.* (citing a 2018 study from Goldman and Lakdawalla and a 2018 study from the Council of Economic Advisers).

117. *Id.* at 1.

118. *Id.* at 5.

119. *Id.*

120. Tomas Philipson is the Daniel Levin Professor of Public Policy Studies Emeritus at the University of the Chicago Harris School of Public Policy and directs the Becker Friedman Institute's Program on Foundational Research in Health Care Markets and Policies. *Thomas Philipson*, UNIV. CHI. HARRIS SCH. OF PUB. POL'Y, https://harris.uchicago.edu/directory/tomas-

calculations and found estimates 550 to 1024 percent greater than that of the CBO's original numbers.[121] Philipson and Durie estimate that the price controls put forth by President Biden would result in a 30 to 60 percent decrease in R&D expenditure and pharmaceutical innovation (upwards of $2 trillion), resulting in a loss of 37.5–100 million life years.[122] For context, this would be ten to twenty times greater than the loss of American life due to the COVID-19 pandemic.[123] It would therefore be unwise to disrupt the success of the world leaders of pharmaceutical innovation by implementing such price regulations.

D. Patent Modifications

A final recurring solution among policy proposals to address high prescription drug prices in the United States is the revision of the patent system for pharmaceuticals. Such proposals include but are not limited to: (1) varying the patent life based on the degree of drug innovation, (2) eliminating patent thickets by removing the exclusive right to use inventions in upstream research, and (3) prohibiting pay-for-delay agreements.[124] There have also been calls for more blanket changes to the patent system such as reducing the duration of patent protection entirely for all pharmaceuticals.[125] The first of the above proposals seems logistically impossible; how does one objectively quantify and measure degrees of innovation? However, questions concerning degrees of innovation are raised in conjunction with the need to eliminate patent thickets under the umbrella of the term "evergreening."[126] Evergreening is a term with a negative connotation used by critics to describe the process of obtaining patents for minor modifications of an existing drug and allegedly delaying the introduction of generics to the market.[127]

The major pushback against evergreening is based on claims that companies are simply looking for economic, rather than therapeutic, advantages,[128] or that discoveries should be truly inventive

philipson [perma.cc/K4ES-SWTE] (last visited Mar. 11, 2023). Troy Durie is a data analyst at the University of Chicago and former member of the Council of Economic Advisors for the White House. *See Troy Durie*, LINKEDIN, https://www.linkedin.com/in/troy-durie-719310a5/ [perma.cc/GXU8-93KB] (last visited Feb. 20, 2023).

121. Philipson & Durie, *supra* note 113, at 6.

122. *Id.* at 7 (citing a 2019 study by the Council of Economic Advisors).

123. *Id.* at 1 (as of September 2021).

124. Alexander et al., *supra* note 43, at 1473.

125. *See* Rajkumar, *supra* note 6, at 2.

126. Collier, *supra* note 87.

127. *Id.*

128. *Id.*

to deserve a patent, not just incremental improvements.[129] Such improvements include creating a new dosage, combination, or formulation unrelated to effectiveness.[130] Patent thicketing is another term used as an example of "patent abuse," whereby manufacturers take out as many patents for a single product as possible.[131] Tahir Amin, the cofounder of the Initiative for Medicines, Access & Knowledge, criticizes manufacturers for "filing large numbers of follow-on or secondary patents to extend their monopolies."[132] On the topic of insulin in particular, the Congressional Diabetes Caucus led by Representatives Diana DeGette (D-CO) and Tom Reed (R-NY) suggested that "Congress could pursue legislation requiring drug manufacturers to show that new formulations of insulin result in improved disease management when compared to current insulin formulations."[133] However, these approaches seek to differentiate improvements to existing drugs solely on effectiveness, which is not the only measure of value in prescription drugs.

As for pay-for-delay agreements, these have less to do with patent protection itself and more to do with marketplace agreements between brand-name and generic manufacturers but are nonetheless considered "payment patent settlements."[134] Under these agreements, generic manufacturers accept payment from brand-name manufacturers who own expired patents, and in return generic manufacturers agree to delay production of generic versions of said off-patent products.[135] California has banned such deals,[136] and the Supreme Court held in *Federal Trade Commission v. Actavis* that such deals *could* be challenged as anticompetitive.[137] However, California's statute is currently subject to a constitutional challenge in court for its ban on pay-for-delay deals under the allegation that such a ban

129. *See* Amin, *supra* note 39.

130. HENRY A. WAXMAN, BILL CORR, JEREMY SHARP, RUTH MCDONALD & KAHAARI KENYATTA, GETTING TO LOWER PRESCRIPTION DRUG PRICES: THE KEY DRIVERS OF COSTS AND WHAT POLICYMAKERS CAN DO TO ADDRESS THEM 42 (Commonwealth Fund ed., 2020), available at https://www.commonwealthfund.org/sites/default/files/2020-10/Waxman_GettingtoLowerRx-Prices_report_v3.pdf [perma.cc/EU8M-JT72]

131. *Id.*

132. Amin, *supra* note 39.

133. DIANA DEGETTE & TOM REED, INSULIN: A LIFESAVING DRUG TOO OFTEN OUT OF REACH 2 (Congressional Diabetes Caucus 2018), available at https://docs.house.gov/meetings/IF/IF02/20190402/109502/HHRG-116-IF02-20190402-SD001.pdf [perma.cc/BDL9-L85P].

134. *See* Alexander et al., *supra* note 43, at 1473; *id.* at 18.

135. DeGette & Reed, *supra* note 133, at 18.

136. Deb & Curfman, *supra* note 98.

137. *See* Fed. Trade Comm'n v. Actavis, Inc., 570 U.S. 136, 140 (2013).

interferes with interstate commerce.[138] For whatever reason, restrictions on pay-for-delay deals fall under the umbrella of patent reform; yet, in an effort to reduce drug prices, such restrictions may not even be constitutional.[139] Either way, generic manufacturers ultimately choose to accept such payoffs to delay market entry in exchange for money; the onus isn't entirely on the patent-holding brand-name manufacturers.

Blame has also been placed on the patent system by way of executive and legislative action in Washington D.C.[140] For example, President Biden's Executive Order claims that "patent and other laws have been misused to inhibit or delay competition from generic drugs."[141] This same Order seeks to end government-granted monopolies for manufacturers who charge prices that are higher than the median prices at which the drugs are available in other countries.[142] Complete agency implementation of such instructions is blatantly contradictory to the purpose of patents, would essentially eliminate all pricing benefits that manufacturers receive under patent protections, and would destroy any form of incentive to be the world leaders in pharmaceutical innovation. Calls for patent reform litter the many proposals by the government and interest groups to reduce prescription drug prices, and while other solutions are at least worth brief considerations, actions against the patent system and the protections it offers to pharmaceutical companies must be rejected without hesitation.

IV. PRESERVING PATENT PROBITY

While the need to reduce prescription drug prices in the United States is obvious, efforts to achieve this should stray far away from the patent system. Proposals that seek to amend patent protections for pharmaceutical innovations will ultimately cause more long-term harm. These efforts are backed by overstated and dramatized claims of patent abuse and evergreening.[143] These claims also fail to acknowledge

---

138. Deb & Curfman, *supra* note 98; *see* Ass'n for Accessible Meds. v. Bonta, 562 F. Supp. 3d 973, 977, 983 (E.D. Cal. 2021), *modified*, No. 2:20-CV-01708-TLN-DB, 2022 WL 463313, at *1–9 (E.D. Cal. Feb. 15, 2022) (enjoining California from enforcing AB 824 with the exception of those agreements completed within California's borders).

139. *See, e.g., Ass'n for Accessible Meds.*, 562 F. Supp. 3d at 977, 987.

140. *See, e.g.*, Exec. Order No. 14,036, *supra* note 24.

141. *Id.*

142. *Id.*; *see also* S. 909, 117th Cong. (2021).

143. Kristina M. L. Acri, *The Importance of Protecting Incremental, Improvement Innovation*, IPWATCHDOG (Oct. 17, 2013, 7:45 AM), https://ipwatchdog.com/2013/10/17/the-importance-of-protecting-incremental-improvement-innovation/id=45725/ [perma.cc/GT23-A3DJ].

that all innovation is valuable, whether it is the development of an entirely new treatment or an improvement of an existing therapy.[144] Sebastian Lohse of the International Chamber of Commerce firmly believes, with the agreement of countless other scholars, that innovation is "a crucial determinant of economic growth and a means to address global challenges."[145] Evergreening, as presented with its pejorative connotation, is founded on two fallacies: (1) that patents protecting incremental innovation are illegitimate and (2) that such improvements delay generic competition.[146] Neither are correct, however, and safeguards already exist within the patent system to prevent the "abuse" referenced by critics.

A. Patents Are Already Safeguarded from Abuse.

The patent system in the United States and that of the Trade-Related Aspects of Intellectual Property (TRIPs) Agreement with the World Trade Organization already contemplate such "abuse" alleged under the guise of evergreening or patent thickening.[147] US policy on patents aims to treat all patents equally, regardless of subject matter, national origin, and the like, and the United States' "unitary patent system" subjects all applications to the same requirements of scope, duration, novelty, etc.[148] Article 27 of the TRIPs Agreement echoes this sentiment, requiring that "patents shall be available and patent rights enjoyable *without discrimination*" while also permitting member states to prohibit patent protections whose commercial exploitation is contrary to *ordre public* or morality.[149] Therefore, while the term evergreening is thrown around in allegations of patent abuse, pharmaceutical manufacturers are still subject to the same requirements for patent protection in every single application they file, and US patent policy and the TRIPs Agreement reject the notion of differential treatment of pharmaceutical patents from those of other

144. *Id.*

145. Sebastian Lohse, *The Importance of Fostering Incremental* Innovation, INT'L CHAMBER OF COM. 1, 5 (2018).

146. Acri, *supra* note 143.

147. Robert Stoll, *The New U.S. Essential Patents Statement—Safeguarding the Integrity of the Patent System*, IPWATCHDOG (Mar. 30, 2020, 1:02 PM), https://ipwatch-dog.com/2020/03/30/sep-statement-integrity-patent-system/id=120250/ [perma.cc/BXN4-W5CF]; *see also* TRIPS: Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 299 [hereinafter TRIPS Agreement].

148. Stoll, *supra* note 147.

149. TRIPS Agreement, *supra* note 147 (emphasis added).

industries.[150] If applying for patent protection of an incremental innovation is just as challenging as it is with so-called radical innovations, where exactly is the abuse described in evergreening or patent thickening?

All innovations, whether radical or incremental, are still required to meet all patentability standards, including novelty, nonobviousness, and utility.[151] Furthermore, the Hatch-Waxman Act permits the extension of market exclusivity by three years for incremental changes, but only when essential clinical trials are conducted.[152] So while evergreening is portrayed as a complete abuse of the patent system whereby manufacturers gain massive monopolies through only minor improvements to existing drugs, as suggested above, the truth remains that these incremental changes receive only three years of protection and are still subject to lengthy, expensive, and risky clinical trials before any protection is granted.[153]

B. Incremental Innovation Is Vital to the Furtherance of Global Health Care.

The scrutiny surrounding the protection of incremental innovation also fails to see that "radical innovation" in technology usually arises from the accumulation of incremental improvements, and contrary to what critics believe, incremental innovation can in fact create greater cost efficiency of a particular product.[154] Nor does such innovation delay generic competition.[155] One study conducted in 2000 found that incremental innovations were usually brought to market at a discount upwards of 70 percent lower than the pioneer and created further competition within a given therapeutic class that resulted in lower prices.[156] Follow-on products also have no bearing on the production of generics for prior versions of any given drug; doctors are still permitted to prescribe generic versions of older products.[157]

When pharmaceutical companies apply for patents on improved versions of their own drugs—the basis of allegations of evergreening—these companies actually progress the pharmaceutical

150. Stoll, *supra* note 147; TRIPS Agreement, *supra* note 147.
151. Stoll, *supra* note 147.
152. CBO, *supra* note 42.
153. *See id.*
154. Lohse, *supra* note 145.
155. Acri, *supra* note 143.
156. *Id.*
157. Collier, *supra* note 87.

industry.[158] These small steps are tantamount to the creation of blockbuster drugs—radical innovations—while also "adding to a drug class, increasing competition among drugs, and creating a stimulus for further innovation."[159] One example of many is the development of beta-blockers, whereby incremental innovation has armed physicians with the ability to individualize treatment of their patients.[160] The original patented beta-blocker drug was propranolol, and incremental innovation has now optimized therapeutic effectiveness and safety of the drug, with differences in dosing schedules, sympathomimetic activity, and vasodilation, for example.[161] This innovation has also added features not originally present such as selective targeting of the B1 receptor and the preservation of blood flow to and from the kidneys.[162] The importance of incremental innovations that result in follow-on drugs is also evidenced by the World Health Organization's Essential Drug list, where 63 percent of listed products are follow-on drugs that resulted from incremental innovation.[163]

Evergreening and the distaste for incremental innovations are most prevalent in countries such as India, where such innovations are required to demonstrate improved efficacy as a minimum standard.[164] Paul Herrling, the chair of the board of the Novartis Institute for Tropical Diseases, believes that if a modification does not provide any advantage to a patient, it should not be granted protection.[165] However, India's concept of evergreening is "overreaching" because it fails to consider the benefit of improvements that result in improved patient safety, reductions in adverse effects, or increases in adherence—all of which are improvements that merit patent protection but would not necessarily meet India's standard of improved efficacy.[166] Herrling's perspective is countered by those such as renowned IP attorney and

158. Albert I. Wertheimer & Thomas M. Santella, *Pharmaceutical Evolution: The Advantages of Incremental Innovation in Drug Development*, COMPETITIVE ENTER. INST. Apr. 2009, at 4.

159. *Id.* at 2. The National Research Council has observed that "the cumulative effect of numerous minor incremental innovations can sometimes be more transforming and have more economic impact than a few radical innovations or [t]echnological breakthroughs." *Id.*

160. *Id.* at 12.

161. *Id.* New versions stemming from the original product include atenolol, bisoprolol, metaprolol, and betaxolol, among others. Each product has different characteristics, including once-daily dosing, equal effectiveness among racial groups, very low central nervous system penetration, etc. *Id.* at 12–13.

162. *Id.* at 12.

163. Acri, *supra* note 143.

164. Collier, *supra* note 87.

165. *Id.*

166. *Id.*

senior partner at Norton Rose Fulbright Canada LLC, Patrick Kierans, who strongly advocates for patent protection for incremental innovations, claiming that if a tweak advances medical science in any way, it should receive a patent.[167] The advancement of science deserves rewarding, plain and simple.[168] An underappreciation of the importance and benefits of incremental innovation does give traction to evergreening claims scattered throughout patent reform movements, but such a "head in the sand" approach is willfully ignorant and likely to do more harm than good, especially if the only goal is to reduce drug prices.

C. Incentives Are the Start, Middle, and End of Pharmaceutical Innovation.

Even with the benefits granted to the generic drug industry by the Hatch-Waxman Act, generic manufacturers face incentive issues because cheap, generic versions of old formulations often have insufficient market power.[169] There exists little appeal to invest in replicating outdated treatments that are no longer the standard of care.[170] Where there is no financial incentive, these generic manufacturers do not pursue development. This same issue would arguably apply to all pharmaceutical manufacturers if proposed reforms to the patent system are passed through legislative efforts to reduce drug prices.

Incentive is the key to innovation, and this statement could not be more true in pharmaceutical development.[171] The patent system is the most successful way of promoting innovation, and there are no good alternatives to patent protection and the benefits it confers.[172] Dr. Kristina Acri, a Professor of Economics at Colorado College, has devoted her research to the economics of patent protections and their alternatives, finding that a shortsightedness exists in those who advocate for strong reductions in patent protection.[173] She asserts that a disconnect exists because pharmaceutical products are so important to human health and well-being, and the fact that pharmaceuticals is a commercialized industry is troubling to some people.[174] However,

167. Collier, *supra* note 87, at E386.
168. *Id.*
169. Rajkumar, *supra* note 6.
170. *See* Greene & Riggs, *supra* note 5, at 1173; *see also* Rajkumar, *supra* note 6, at 1–2.
171. Interview with Dr. Kristina Acri (Dec. 12, 2021) [hereinafter Acri Interview].
172. *Id.*
173. *Id.*
174. *Id.*

flawed reasoning is bound to follow when focusing purely on the health benefits of these products and ignoring where they came from and what incentivized them into existence.[175] Efforts to constrain patent protections demonstrate a failure to acknowledge that without any financial incentive, pharmaceutical products will likely not be invented or invested in.[176] The only way for pharmaceutical research to continue, which unavoidably includes the associated costs and risks, is the provision of substantial rewards granted through the patent system.[177] At the end of the day, pharmaceutical companies are businesses that exist to improve society upon the caveat of a profit margin, just like most companies in capitalist economies; without these businesses, the flow of new or improved medicines would slow massively.[178]

An understanding of the risks and rewards in pharmaceutical developments is key in this debate. Bringing new drugs to market carries "Vegas-like odds," and putting up barriers to obtaining intellectual property protections will only discourage innovators from taking those risks.[179] The patent system, originating with the Statute of Monopolies,[180] recognizes the economic benefits from encouraging people to take these risks and bring new things forward, but as Patrick Kierans claims, "[a] week doesn't go by when you don't open up a newspaper and see that some company's drug got wiped out in a phase-3 clinical trial, and by that time they had already sunk 800 to 900 million bucks into that drug."[181] The average price of bringing a new drug to the market is so high, and the average success rate of doing so is so low, that massive incentives are the only way to encourage pharmaceutical innovation.[182] In fact, even with the current protections as they are, seven of ten marketed medicines do not recoup the cost of R&D and are therefore manufactured and sold at a loss.[183] The risk-reward analysis is also an explanatory factor for the frequency of incremental innovation that so commonly gets a bad rap under the name of evergreening.[184] The pharmaceutical industry is so competitive and is under such constant scrutiny that firms look to reduce risks

175. *Id.*

176. *Id.*

177. Vagelos, *supra* note 35, at 1083.

178. *Id.*

179. Collier, *supra* note 87, at E386.

180. Statute of Monopolies, 1623, 21 Jac. 1, c. 3, § 6 (Eng.) (a 1623 Act of the Parliament of England known as the first statutory expression of English patent law).

181. Collier, *supra* note 87, at E386.

182. *Id.*

183. Vagelos, *supra* note 35, at 1082.

184. Wertheimer & Santella, *supra* note 158, at 16.

without impacting revenues, hence the occurrence of low-risk incremental innovations.[185] Dr. Albert Wertheimer, a veteran in sociobehavioral and administrative pharmacy research, puts forth a trade-off that currently exists in the pharmaceutical industry: "would we rather have fewer pharmaceutical companies investing huge capital in high risk projects that are more likely to fail than succeed, or many pharmaceutical companies with diversified pipelines investing in safer incrementally innovative drugs that reduce risk, therefore providing the capital for investment in more risky endeavors?"[186]

A majority of medicines are developed in the United States because other countries have price controls and reduced incentives, and innovation cannot take place in those environments; if pharmaceutical development is not profitable in the United States, it certainly won't happen anywhere else.[187] Adamantly stated then, efforts to reduce prescription drug prices in the United States must not implicate changes to the patent system or the protections it confers. The incentives offered to pharmaceutical manufacturers to further the treatment of disease and illness are irreplaceable, and innovation—both radical and incremental—is valuable and should be protected, not reigned in through ill-considered efforts to reduce prescription drug prices.

V. WHAT OPTIONS ARE WORTH CONSIDERING?

Many of the proposals put forth within the government and by various interest groups appear to focus on addressing high prices on the back end, once the drug has been produced and manufacturers begin setting prices.[188] The promotion of biosimilars or generics to bring prices down through competition is a potential solution that looks to address prices once products are already on the market.[189] Passing legislation that requires greater transparency from manufacturers about their drug pricing with hopes of negotiating lower prices, especially when compared to prices abroad, also seeks to address the problem once a product has been developed.[190] Government regulation and price caps do target prices earlier in the process, but still do not have any effect until after a drug has been developed and costs are already sunk.[191]

185. *Id.* at 6.
186. *Id.* at 18.
187. Acri Interview, *supra* note 171.
188. Deb & Curfman, *supra* note 98.
189. *See, e.g.*, van de Vooren et al., *supra* note 69.
190. *See, e.g.*, Bailey, *supra* note 52.
191. *See, e.g.*, Vagelos, *supra* note 35, at 1080.

Separate from the above proposals, however, reducing patent protections for pharmaceutical manufacturers is fraught with the backing of ill-informed, fallacious, and "short-termist" claims, and such action must be avoided altogether. What options remain then?

Perhaps by working with manufacturers, rather than vilifying them and clipping their wings, the government may be able to lower prescription drug prices on the front end. If manufacturers price their drugs in accordance with R&D costs of the drug, corporate overhead, administrative and regulatory costs, and marketing, and allow room for profit, why not seek to lower input costs? Even though very few drugs recoup the costs of their development,[192] manufacturers still price their drugs with hopes that at least some of their expenditures are recovered. Why not reduce the amount that a manufacturer would need to recover then? R&D costs what it costs,[193] and overhead capital must remain to maintain the companies and pay their employees. In fact, Merck reported that nearing the turn of the century, the company had 4,500 people in research at any one time developing new drugs, totaling over one million hours over a six-week period.[194] Administrative and regulatory costs are beyond the control of manufacturers too. Perhaps offering tax rebates or other cost-saving, government-issued programs to reduce total manufacturer expenditures would achieve drug pricing goals.

One aspect of front-end cost cutting proposed in recent legislation is the elimination of direct-to-consumer (DTC) marketing, which would in turn reduce expenditures on marketing and thus reduce prices to some extent.[195] If not completely abolishing the practice, then at least reducing its use could lower expenditure.[196] DTC marketing allows pharmaceutical companies to advertise directly to consumers;[197] however, this practice is currently only permitted in the United States

192. *Id.* at 1082.

193. Increasing R&D input is a necessary aspect for the development of new medicines, reflecting the obvious positive correlation between R&D input and innovation in any industry, hence why R&D costs is a variable that certainly cannot be reduced in a society that seeks new cures and new treatments. *See id.*

194. *Id.* at 1081.

195. *See* H.R. 4278, 117th Cong. (2021); S. 2304, 117th Cong. (2021) (directing the Comptroller General to study the effects of DTC on drug costs and requiring price disclosure in DTC ads).

196. Alexander et al., *supra* note 43, at 1475.

197. Robert H. Shmerling, *Harvard Health Ad Watch: How Direct-to-Consumer Ads Hook Us*, HARV. HEALTH PUBL'G (Mar. 3, 2022), https://www.health.harvard.edu/blog/harvard-health-ad-watch-what-you-should-know-about-direct-to-consumer-ads-2019092017848 [perma.cc/G3AH-AL4N].

and Australia.[198] The practice was banned in the United States until 1997, at which point the FDA lifted restrictions.[199] Since then, spending on advertising by pharmaceutical companies has soared to nearly $10 billion per year, which some allege drives up health care costs without adding tangible health benefits.[200] With a majority of manufacturers spending about the same on marketing as they do research according to some studies, the elimination of DTC marketing could have a significant impact on reducing drug costs.[201] However, there is very little public data on DTC advertising, and it is therefore difficult to tease out from other marketing efforts.[202] Dr. Acri suggests there is a good reason to believe that pharmaceutical companies would see an end to DTC marketing, thus matching the rest of the world, but claims there currently exists a game of one-upmanship between manufacturers with no company willing to back down first.[203] Whether there is any correlation whatsoever between DTC and drug prices remains to be seen (hence legislative proposals such as H.R. 4278),[204] but many are quick to suggest that DTC marketing is wasteful and the health care landscape would be cheaper without it.[205] Reducing input costs or expenditures for manufacturers on the front end would reduce the amount that companies seek to recover and in turn remove the need to price drugs to the level at which they currently are.

Subsequently, perhaps the discussion is best focused on methods to supplement the incentives of the patent system—not necessarily reducing costs, but still lowering the amount manufacturers would seek to recover. IP experts and economists alike, including Dr. Acri, suggest the idea of supplemental incentives through nationally or internationally awarded prizes for particular treatments.[206] While the technicalities of such an award system would require substantial consideration among this country's leaders or the world's leaders,

198. Bailey, *supra* note 52.

199. Shmerling, *supra* note 197.

200. *Id.*

201. Bailey, *supra* note 52.

202. Acri Interview, *supra* note 171; *see* Tim K. Mackey, Raphael E. Cuomo & Bryan A. Liang, *The Rise of Digital Direct-to-Consumer Advertising?: Comparison of Direct-to-Consumer Advertising Expenditure Trends from Publicly Available Data Sources and Global Policy Implications*, 15 BMC HEALTH SERVS. RSCH. 1, 8 (2015).

203. *Id.*

204. H.R. 4278, 117th Cong. (2021).

205. Acri Interview, *supra* note 171.

206. *See, e.g.*, Michael Kremer & Heidi Williams, *Incentivizing Innovation: Adding to the Tool Kit*, 10 U. CHI. PRESS 4 (2010).

developing a way to separate the price of a drug from the price of innovation should be the overarching goal to reduce drug prices.[207]

Michael Kremer, Nobel Prize Winner and now a faculty member at the University of Chicago, has been a large proponent for supplemental incentives to reduce drug prices for over a decade now, as evidenced in his publication with the National Bureau of Economic Research.[208] He too notes a resurgence of concern over drug costs from resulting patent protection and outlines proposals that could supplement patent rights, reducing costs while "limiting the risk of undermining the expectations of reward critical to the current [intellectual property rights] system."[209] One such supplement is the offering of prizes, whether monetary or otherwise. The United States recently implemented the fast-track regulatory approval incentive,[210] where in exchange for developing a treatment for a neglected disease, FDA approval would be expedited.[211] This type of prize would also come at a low cost to the government, while saving manufacturers time and money in the delay of getting FDA approval.[212] Whether it is a "push program" that would provide upfront support for R&D inputs, or a "pull program" that rewards successful products upon completion, such programs would supplement the incentives of the patent system and help separate the price of the product from the price of innovation, likely reducing prescription drug prices.[213]

Irrespective of the array of scattered proposals that claim to be the solution to high prescription drug prices, the best solution would involve working with manufacturers on the front end of innovation to bring their costs down. Whether that is through tax rebates, prize pools, or push or pull programs that supplement the incentives of the patent system, the lower the dollar amount that manufacturers seek to recoup from product sales, the less they will have to charge for their products.

VI. CONCLUSION

The need to lower prescription drug prices for consumers in the United States grows each year and with each new drug that comes to

207. *Id.* at 6.

208. *Id.*

209. *Id.* at 1.

210. This proposal was made in 2006 by David Ridley, Henry Grabowski, and Jeffrey Moe, faculty at Duke University and members of the Global Health Institute. *Id.* at 5.

211. *Id.*

212. *Id.*

213. *Id.*

market.[214] Take the insulin that many diabetics need to survive, for example. An estimated one in four diabetics are currently forced to ration their insulin or skip doses because costs can surpass $1,000 per month.[215] The issue is not limited to insulin either; across all prescription medications, prices in the United States are 256 percent higher than all other OECD countries combined.[216] With the average cost of developing a new drug now surpassing $3 billion, taking over a decade to complete, and with only about 10–20 percent of FDA-reviewed drugs even making it to market, it comes as no surprise that pharmaceutical companies are forced to price their products as they do in order to recover at least a portion of their expenditures.[217]

Solutions circulating Congress have recommended the promotion of generics and biosimilar versions to bring brand-name prices lower through competition, for example.[218] The efficacy of this solution has proven to be neither consistent nor predictable, however; consumers naturally gravitate towards brand-name products for reputability, biosimilars of large molecule drugs like insulin are staggeringly difficult to develop with minimal decreases in final cost, and generics have been observed to cost more than the originals in some instances.[219] Additionally, generic and biosimilar manufacturers are only permitted to market these alternatives once the originals are no longer under patent protection.[220] However, by the time patents expire, a better, more effective, safer, or cheaper version already exists, and the incentive to develop products below the latest standard of care is sorely lacking.[221]

Other solutions suggest increasing transparency from manufacturers or imposing greater government regulation on pricing.[222] However, reporting requirements risk imposing greater administrative costs on manufacturers, thus increasing the overhead that needs to be recovered from sales of their products, and therefore such requirements may be better targeted towards other actors in the supply chain.[223] Even more concerningly though, imposing greater government regulation and price caps would completely stifle the

214. *See* Rajkumar, *supra* note 6, at 2.
215. Barker, *supra* note 1, at 312, 316.
216. MULCAHY ET AL., *supra* note 7, at xv.
217. *See* Rajkumar, *supra* note 6, at 2; *see also* Vagelos, *supra* note 35, at 1083.
218. *See, e.g.*, van de Vooren et al., *supra* note 69, at 127.
219. *See* Iacocca & Vallen, *supra* note 33, at 551; *see also* CBO, *supra* note 42.
220. Greene & Riggs, *supra* note 5, at 1173.
221. *Id.*
222. Bailey, *supra* note 52; *see also* Deb & Curfman, *supra* note 98.
223. *See* Iacocca & Vallen, *supra* note 33.

innovation that occurs in the United States.[224] Most pharmaceutical innovation in the world takes place in the United States, and much of the infrastructure needed for development and testing is found here too.[225] This, however, is a facet of a free enterprise system with significantly less government regulation and the absence of price caps.[226] If the United States were to mirror the regulations and price caps imposed by other countries around the world, the rate of innovation in the United States would come to match that of other countries around the world: significantly limited.[227] If there is ever a hope for curing cancer, for example, stifling the rate of innovation is not the way to go.

The proposed solution to high prescription drug prices that would be most harmful, however, is the imposition of restrictions or pullbacks on the patent system. Patent protection is the best incentive for pharmaceutical development; nothing else even comes close.[228] Pharmaceutical manufacturers are, like any other company in a capitalist economy, spurred onward by the ability to help society on the contingency of a profit margin.[229] Pharmaceutical development, trial, and marketing becomes more expensive with each successive year, and without the ability to recover at least some of these expenditures, no company would ever invest in the expensive process to begin with.[230] As for the fallacious issue of evergreening, surely society would seek to reward manufacturers for creating better, safer, more effective versions of prescription drugs. The willingness today of a diabetic to take insulin from 1923 is likely minimal, and why? Because manufacturers have developed better and safer insulin. But these innovations were not free, so why ban the award of patent extensions for incremental innovation?

Thanks to the availability of incentives for product improvements and follow-on drugs, diabetes treatment, for example, can include an individualized approach of insulin therapy that improves patients' glycemic control, minimizes hypoglycemic risk and side effects, conjugates their preferences, and increases their adherence to the treatment.[231] The key to all innovation is incentive, and taking

224. Vagelos, *supra* note 35, at 1080.

225. Bailey, *supra* note 52.

226. Iacocca & Vallen, *supra* note 33, at 528; Vagelos, *supra* note 35, at 1081.

227. *See* Philipson & Durie, *supra* note 113, at 4–8.

228. Acri Interview, *supra* note 171.

229. *Id.*

230. *Id.*

231. Ignazio Vecchio,Cristina Tornali, Nicola Luigi Bragazzi & Mariano Martini, *The Discovery of Insulin: An Important Milestone in the History of Medicine*, 9 FRONTIERS IN ENDOCRINOLOGY 1, 7 (2018).

away incentive is ruinous.[232] Michael Kremer aptly notes that "economic growth depends on technological progress, and the nonrival nature of scientific knowledge generated by research and development implies that institutions beyond competitive markets are required to promote innovation," with patents being one such institution.[233]

Therefore, the solution is perhaps to work with pharmaceutical companies, encouraging and rewarding innovation rather than maligning manufacturers for trying to recover a fraction of the billions of dollars they have expended developing a drug. The most common theme among the proposals discussed above is that they seek to reduce prices after a drug has already been developed, after the billions of dollars have already been expended.[234] Perhaps by working with manufacturers rather than against them, costs can be reduced prior to the development of a drug, so that a manufacturer has less to recover from market exclusivity benefits awarded by patent protection. Some have suggested returning to a pre-1997 ban on DTC marketing, reducing some of the costs associated with bringing a drug to market.[235] Others have suggested supplemental rewards that ensure manufacturers a given amount of monetary compensation upon the development of a certain drug.[236] Regardless of where pharmaceutical manufacturers can save money, or how the incentives of the patent system can be supplemented, these companies should not be punished for creating medicines and developing or improving treatments for many of the ailments that plague modern society. A hard line must be drawn to protect the patent system, because without incentivizing innovation, the currently untreatable ailments that cause so much strife within families and communities today will never be cured.

Alexander Wharton[*]

232. Acri Interview, *supra* note 171.

233. Kremer & Williams, *supra* note 206, at 1.

234. *See supra* Section III.

235. Bailey, *supra* note 52.

236. *See* Kremer & Williams, *supra* note 206, at 7–8.

[*] JD Candidate, Vanderbilt Law School, 2023. The Author would like to thank Meredith Capps for her guidance initiating the writing process, Christina Acri for her interview and perspectives which hugely shaped this Note, and the editorial staff of the *Vanderbilt Journal of Entertainment and Technology Law* for developing this Note into its final form.