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NOTES

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INTRODUCTION

Global sales of pharmaceuticals reached over $1 trillion annually each of the past three years and the trajectory of growth is expected to continue in the coming years.[1] In the United States alone, pharmaceutical sales topped $500 billion in each of the past two years, making it the largest market in the world.[2] The importance of the pharmaceutical market was thrust into the spotlight during the COVID-19 pandemic, as both policymakers and individual companies raced to provide access to life saving medicine to those in need. Large pharmaceutical companies engaged in partnerships with small research start-ups, developing breakthrough vaccines that reached the market in record time.[3] Two of the leading vaccine manufacturers, Pfizer and Moderna, are projected to approach $50 billion in sales in 2022 alone.[4]

News publications have been replete with headlines about astronomically high costs to consumers for essential treatments over the past decade, featuring stories about EpiPens and insulin.[5] The increase

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[1] Matej Mikulic, *Global Pharmaceutical Sales from 2017 to 2021, By Region,* STATISTA, (Jul. 27, 2022), https://www.statista.com/statistics/272181/world-pharmaceutical-sales-by-region/.

[2] *See id.*

[3] Desma Polydorou et al., *Transatlantic Enforcers Working Group on Pharmaceutical Mergers: Reimagining Innovation May Have Side Effects*, 36 ANTITRUST 70, 70 (2021).

[4] Spencer Kimball, *What's next for Pfizer, Moderna, beyond their projected $51 billion combined Covid vaccine sales this year*, CNBC, (Mar. 3, 2022, 6:13 PM), https://www.cnbc.com/2022/03/03/covid-pfizer-moderna-project-51-billion-in-combined-vaccine-sales-this-year.html.

[5] *See, e.g.*, Lisa Rapaport, *Another look at the surge in EpiPen costs,* REUTERS, (Mar. 27, 2017, 6:03 PM), https://www.reuters.com/article/us-health-epipen-costs/another-look-at-the-surge-in-epipen-costs-idUSKBN16Y24O (explaining how generic drugmaker Mylan increased the list price of the EpiPen from $94 to $609, resulting in a 535 percent price hike for patients out-of-pocket spending from 2007 to 2014); Steve Inskeep & Allison Aubrey, *Insulin costs increased 600% over the last 20*

in innovation and resulting market dominance of large pharmaceutical companies has brought with it renewed scrutiny from regulators about pricing concerns. In response to increasing prescription drug prices for many Americans, President Biden and Congress worked to include drug pricing reform in the Inflation Reduction Act of 2022 ("IRA").[6] Under the IRA, the Secretary of the Department of Health and Human Services is empowered to establish a "Drug Price Negotiation Program," under which he shall negotiate prescription drug prices and enter into agreements with manufacturers of selected drugs.[7] Regardless if it were the correct normative approach to reduce prices for consumers, the current administration took a substantial step to address the concern over individual social welfare, likely coming at the expense of future profits for pharmaceutical companies.

Amidst concerns over future regulation and the sustainability of profits from existing products, pharmaceutical companies have turned largely to mergers and acquisitions ("M&A") to supplement their own internal research and development ("R&D") and to find the next "blockbuster" drug. Over the past few decades, spending on R&D has increased dramatically, and on average, pharmaceutical companies spent approximately one quarter of their revenues on R&D in 2019.[8] The disproportionate spending on R&D appears logical when considering the "costly and uncertain process" of developing a drug that passes all milestones during clinical trials and is granted approval by the United States Food and Drug Administration ("FDA").[9] According to research done by the Congressional Budget Office, only 12 percent of drugs that enter clinical trials are approved by the FDA, and the cost of R&D spending on an individual approved drug can be as high as $2 billion.[10] Large pharmaceutical companies have turned to small biotechnology

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years. States aim to curb the price, NPR, (Sept. 12, 2022, 5:07 AM), https://www.npr.org/2022/09/12/1122311443/insulin-costs-increased-600-over-the-last-20-years-states-aim-to-curb-the-price#:~:text=The%20price%20of%20insulin%20remains,patients%20ration%20this%20lifesaving%20drug (discussing how insulin manufacturers have increased prices by 600% over the course of the past twenty years).

[6] *The Inflation Reduction Act Lowers Health Care Costs for Millions of Americans*, CTR. FOR MEDICARE & MEDICAID SERV., (Oct. 5, 2022), https://www.cms.gov/newsroom/fact-sheets/inflation-reduction-act-lowers-health-care-costs-millions-americans.

[7] 42 U.S.C. § 1320f.

[8] *Research and Development in the Pharmaceutical Industry*, CONG. BUDGET OFF. 1 (Apr. 2021), https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf. The share of revenue devoted to R&D expenses is larger than other innovative industries, including the expenses for "semiconductors, technology hardware, and software."

[9] *Id.* at 2.

[10] *Id.*

startups and partnerships with nonprofit research institutions as a means of outsourcing R&D to those who have the ability to specialize on certain biological processes or individual small molecules, and have the flexibility to research in the manner they see fit.[11] Given the high cost associated with developing new drugs, and the risk of failure in one or more stages of development, smaller startup companies are incentivized to engage in transactions with larger incumbent firms in order to commercialize new products.[12]

While the value of M&A to large pharmaceutical companies and their shareholders has been debated for years, both scholars and regulatory officials have begun to focus on whether consolidation between firms will harm innovation, and thus negatively impact downstream social welfare for individuals.[13] The debate intensified following the release of a working paper by economists Colleen Cunningham, Florian Ederer, and Song Ma, which introduced the concept of "killer acquisitions" – an incumbent firm acquires a nascent competitor with the motivation of terminating development in order to reduce competition to its existing or pipeline products.[14] While subsequent research papers have begun to echo similar concerns over the anticompetitive nature of M&A in the pharmaceutical industry, others have discussed the problems associated with proving such phenomena exist.[15] To explore the issue further, leading antitrust authorities, including the FTC, the European Commission ("EC"), the Department of

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[11] *See* Joanna Shepherd, *Consolidation and Innovation in the Pharmaceutical Industry: The Role of Mergers and Acquisitions in the Current Innovation Ecosystem*, 21 J. HEALTH CARE L. & POL'Y 1, 1–10, (2018); *see also* Constance E. Bagley & Christina D. Tavrnø, *Pharmaceutical Public-Private Partnerships in the United States and Europe: Moving from the Bench to the Bedside* (discussing the encouragement of legally binding partnerships between private pharmaceutical companies and public research institutions or private universities utilizing public grants to incentivize innovation and increase the likelihood of successful commercialization of new drugs).

[12] *See* Shepherd, *supra* note 11, at 9–10.

[13] *Id.* at 1–2.

[14] *See* Collen Cunningham et al., *Killer Acquisitions*, Vol. 129, No. 3 J. POL. ECON. 649 (Mar. 2021).

[15] *See, e.g.*, W. Robert Majure et al., *Evaluating innovation theories of harm in merger review: economic frameworks and difficulties*, CORNERSTONE RSCH., (Aug. 2021), https://www.cornerstone.com/wp-content/uploads/2022/01/Evaluating-innovation-theories-of-harm-in-merger-review.pdf (addressing the difficulties in finding evidence and supporting empirical measurement in proving harm to innovation); Patricia M. Danzon & Michael A. Carrier, *The Neglected Concern of Firm Size in Pharmaceutical Mergers*, 84 ANTITRUST L.J. 487 (2022) (introducing the "neglected concern of firm size" in pharmaceutical mergers and suggesting that antitrust authorities should differentiate between large firms and others when conducting merger review).

Justice Antitrust Division ("DOJ"), the Canadian Competition Bureau, and the United Kingdom's Competition and Markets Authority ("CMA"), issued a notice seeking public comment on how to best inform their approaches to analyzing pharmaceutical mergers.[16]

While the concentration of market power may lead to increased prices in the short term for consumers, antitrust authorities should be wary of examining the deleterious effects on innovation as a standalone theory of harm because countervailing interests in synergy and innovation stemming from pharmaceutical M&A may increase total consumer surplus in the long run.[17] Additionally, the current patent system, which provides a limited term of monopoly for patent holders, and requires companies to license existing products or face liability for patent infringement, provides consistent incentives for large pharmaceutical companies to acquire new products and ideas through acquisition, rather than through organic development.[18] Many startup biotechnology companies develop specifically for the purpose of selling the business in order to profit, instead of adopting the role of a true competitor to larger incumbent firms.[19] In examining the actual effect on competition resulting from an acquisition, the counterfactual world is not observable, and it would be impossible to predict a nascent company's future effects on competition.[20]

Instead, this note will argue that government and regulatory authorities should focus on easing access to downstream innovation by broadening research exemptions to patent infringement. Part I of this note will focus on the current state of patent protection and exclusivity afforded to pharmaceutical companies. Part II will discuss incentives

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[16] *Multilateral Pharmaceutical Merger Task Force Seeks Public Input*, FED. TRADE COMM'N. (May 11, 2021), https://www.ftc.gov/news-events/press-releases/2021/05/multilateral-pharmaceutical-merger-task-forceseeks-public-input. The Task Force sought comment on seven questions on the effects of pharmaceutical mergers. These included: "(1) [w]hat theories of harm should enforcement agencies consider . . .?; (2) [w]hat is the full range of a pharmaceutical merger's effects on innovation?;... and (6) [w]hat types of remedies would work . . .?"

[17] *See generally* Robert D. Cooter & Uri Y. Hacohen, *Progress in the Useful Arts: Foundations of Patent Law in Growth Economics*, 22 YALE J. L. & TECH. 191 (2020). This article outlines that the purpose of the patent law system is to "increase economic growth through innovation." Using the constitutional background as a basis for policy, the authors note that social welfare can increase exponentially from innovation, outweighing any losses from inefficiency or inequality stemming from reallocation of resources.

[18] *See* Matthew J. Higgins & Daniel Rodriguez, *The Outsourcing of R&D Through Acquisitions in the Pharmaceutical Industry*, 80 J. FIN. ECON. 351 (2006).

[19] *See* Cooter & Hacohen, *supra* note 17, at 197–98.

[20] John M. Yun, *Are We Dropping the Crystal Ball? Understanding Nascent and Potential Competition in Antitrust*, 104 MARQ. L. Rev. 613, 636–42 (2021).

created that lead rational actors to engage in M&A instead of through internal R&D. Part III will address the development of innovation as a standalone theory of harm in merger review, and the fallacies associated with labeling certain transactions as "killer acquisitions." Finally, Part IV of the note will look at the intersection of pharmaceutical transactions and intellectual property protection, and how encouragement of collaboration between firms may offset the negative externalities associated with high costs to consumers and terminated R&D projects.

I. EXCLUSIVE RIGHTS IN PHARMACEUTICALS

A. Patent Protection

Congress was granted the power under the Constitution to "promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors the exclusive right to their . . . [d]iscoveries."[21] While the theoretical underpinning for the United States patent system is vague, it is best understood as providing incentives to stimulate innovation and thus improve human welfare.[22] Generally, patent owners are entitled to exclude competitors from "making, using, or selling the patented invention" for a period lasting 20 years after the filing date of the patent application—patents create a short-term monopoly for their holder.[23] The grant of exclusivity is codified in statute under the Patent Act of 1952 ("Patent Act")[24], most recently amended by the Leahy-Smith America Invents Act ("AIA").[25] Under 35 U.S.C. § 101, any person who "invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof . . ." is eligible to qualify for a utility patent.[26] In the context of pharmaceuticals, patents may claim "compounds . . ., a method of using

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[21] U.S. CONST. art. I, § 8, cl. 8.
[22] *See* Christopher Buccafusco & Jonathan S. Masur, *Drugs, Patents, and Well-Being*, 98 WASH. U. L. REV. 1403, 1404 (2021).
[23] *Id.* at 1404–05.
[24] *See generally* Patent Act of 1952, 35 U.S.C. §§ 1–390.
[25] Pub. L. No. 112-29, 125 Stat. 284 (2011). The AIA was a groundbreaking development in US patent law, as it changed the prior "first-to-invent" rules to a "first-inventor-to-file" system. After the effective date of March 16, 2013, priority was given to the inventor who filed her patent application with the United States Patent and Trademark Office ("USPTO"), instead of relying on a claimed date of invention. The USPTO instituted the new system, among other changes, to provide "greater transparency, objectivity, predictability, and simplicity in patentability determinations." *See Examination Guidelines for Implementing the First Inventor to File Provisions of the Leahy-Smith America Invents Act*, 37 C.F.R. Part 1 (2013).
[26] 35 U.S.C. § 101.

the product, a method of making or administering the product, or a very of other patentable inventions relating to a drug or biologic."[27] After filing a patent with the USPTO, a patent examiner will determine if the claimed invention is (1) directed at patentable subject matter, (2) new, (3) nonobvious, and (4) useful.[28]

Once a valid patent has been granted by the USPTO, the holder of the patent has the exclusive right to make, use, sell, or import the invention within the United States until the expiration of the patent term or the patent is invalidated.[29] Thus, any person who "makes, uses, offers to sell, or sells any patented invention" infringes that patent, and may be liable for damages, and may be enjoined from its use.[30] Additionally, a patent holder may license a right in the patent to another, authorize the use of the patented material and waiving liability for patent infringement.[31] Due to the limited duration of exclusive rights to a pharmaceutical compound, and the profitability of exclusive use and marketing, patent holders have strong incentives to enforce their rights, and new competitors (often generic drug manufacturers) seek to invalidate the claimed patent. Under the statutory text, patents are governed by federal law, and federal district courts have jurisdiction in adjudicating any disputes.[32] All appeals from patent matters are heard by the United States Court of Appeals for the Federal Circuit.[33]

While the term for a patent is 20 years starting from the date of application, pharmaceutical companies can apply for patent term adjustments. These modifications to the standard term include time to account for excessive delays in examination at the USPTO, or delay resulting from obtaining marketing approval, typically approval by the FDA.[34] The Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act") sought to address distortions to patent terms associated with obtaining regulatory approval prior to marketing a drug.[35] Since a patent owner loses a period of the patent term following application, but before approval, the owner can apply for a patent term

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[27] *Drug Prices: The Role of Patents and Regulatory Exclusivities*, CONG. RSCH. SERV. 2 (2021) [hereinafter *Role of Patents and Exclusivities*].
[28] 35 U.S.C. § 101–03.
[29] *Role of Patents and Exclusivities*, *supra* note 27, at 25.
[30] 35 U.S.C. § 271(a).
[31] *Id.* at § 271(d).
[32] 28 U.S.C. § 1338.
[33] *Id.* at § 1295(a)(1).
[34] *Role of Patents and Exclusivities*, *supra* note 27, at 26.
[35] United States Patent and Trademark Office, *Patent Term Extension for Delays at Other Agencies Under 35 U.S.C.156*, Manual of Patent Examining Procedure § 2750 (9th ed. 2020).

extension ("PTE").[36] The grant of a PTE shall "not exceed 5 years from the date of expiration of the original patent term."[37]

While claiming a specific compound for the active ingredient within a pharmaceutical product typically provides the broadest breadth of protection, companies often seek to provide additional exclusivity through a variety of other patents. Pharmaceutical companies employ different filing strategies for their patent portfolio, but many apply for patent protection on different features of a drug or biologic beyond the initial claims.[38] These can include:

> 1. Formulations of a pharmaceutical (e.g., an administrable form and dosage, or a combination of active and other ingredients);
> 2. Methods of using the pharmaceutical (e.g., an indication or use of the drug for treating a particular disease);
> 3. Technologies and methods used to administer the pharmaceutical (e.g., an inhaler or injector device);
> 4. Technologies and methods for manufacturing the pharmaceutical (e.g., a manufacturing process); or
> 5. Other chemicals related to the active ingredient, such as crystalline forms, polymorphs, intermediaries, salts, and metabolites.[39]

Critics of strong intellectual property rights under the current system often highlight the multitude of patents on a single pharmaceutical product as an attempt to circumvent the normal patent process to extend the effective life of exclusivity.[40] Two of the most frequently cited criticisms are so-called patent "evergreening" and "patent thickets."[41] Patent "evergreening" is the practice of "filing for new patents on secondary features of a pharmaceutical as earlier patents expire," functionally extending the 20-year term of exclusivity through secondary patents.[42] "Patent thickets" refer to the filing strategy of certain pharmaceutical companies referring to the filing of numerous

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[36] 35 U.S.C. § 156.
[37] *Id.* at § 156(d)(5)(E)(i).
[38] *Role of Patents and Exclusivities*, *supra* note 27, at 28–29.
[39] *Id.* at 29.
[40] *See* Cooter & Hacohen, *supra* note 17, at 193 (explaining recent criticism of patent rights during both the Obama and Trump administration, which led to increased involvement from Congress).
[41] *Role of Patents and Exclusivities*, *supra* note 27, at 2.
[42] *Id.*

overlapping patents for the same pharmaceutical, creating a robust patent portfolio and thereby deterring competition through the risk of infringement.[43]

B. FDA Approval and Regulatory Exclusivity

When considering the development of a new drug or biologic, pharmaceutical companies must comply with the Federal Food, Drug and Cosmetic Act ("FD&C Act"), which governs the manufacture and distribution of pharmaceutical drugs.[44] In order to protect public health, new drugs and biologics must obtain FDA approval before they are marketed within the United States.[45] In order to meet the FDA guidelines, a company must submit a New Drug Application ("NDA").[46] The FDA has three main considerations in approving an application: (1) whether the drug is safe and effective in its proposed use; (2) whether the drug's proposed labeling is appropriate; and (3) whether the methods used in manufacturing the drug are adequate to preserve the drug's identity, strength, quality and purity.[47] While the FDA seeks to encourage and incentivize innovation through new treatments, it must balance the benefits of the proposed treatment with the associated harms and risks to the health of consumers.[48]

Before the drug will ever be introduced to the consuming market, a pharmaceutical company must demonstrate the "drug's safety and effectiveness for humans . . . "through clinical trials."[49] Clinical trials can be burdensome for those seeking approval from the FDA, and the selection of appropriate candidates is often a long and arduous process. Clinical testing occurs in three separate phases: phase I trials introduce the investigational new drug into a small population of humans, and phase II and III trials more thoroughly examine the efficacy of a new drug, and expand the study to a larger number of participants.[50]

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[43] *Id.*
[44] *See* 21 U.S.C. Ch. 9, Subch. V.
[45] 21 U.S.C. § 355(a) (regulating the approval of new drugs before introduction into commerce); 21 U.S.C. § 262(a) (forbidding introduction of biological products into commerce that do not comply with stated terms).
[46] *New Drug Application (NDA)*, FDA (Jan. 21, 2022), https://cacmap.fda.gov/drugs/types-applications/new-drug-application-nda#:~:text=The%20NDA%20application%20is%20the%20vehicle%20through%20which,New%20Drug%20%28IND%29%20become%20part%20of%20the%20NDA.
[47] *Id.*
[48] *Id.*
[49] *Role of Patents and Exclusivities*, *supra* note 27, at 11–12.
[50] For a further breakdown of the phases of clinical studies, *see* 21 C.F.R. § 312.21.

Following the amendment to the FD&C Act in 1962, the size of the population participating in clinical trials has expanded dramatically, making it more difficult to garner support from investors and outside parties.[51] In addition to the size of the trials, "the costs of recruiting patients, the length of the clinical trial period, and the number and complexity of clinical tests used in clinical trials have increased over time."[52] With the increased time and cost associated with clinical trials, it has raised development costs of each new drug to over $2 billion.[53] At the same time, companies have little guarantee of success, as FDA estimates predict that only 10 percent of new drugs entering testing will ever reach the market.[54] As new drugs become increasingly specialized, and courses of treatment reflect personalized characteristics, these requirements will only become more difficult for pharmaceutical manufacturers to meet.[55]

While the hurdles pharmaceutical companies must face to obtain FDA approval remain burdensome, they continue to face competition from non-brand name drug manufacturers (generic manufacturers).[56] Following the passage of the Hatch-Waxman Act, generic drug makers were empowered to compete with brand name pharmaceutical companies through the introduction of the abbreviated new drug application ("ANDA").[57] Instead of having to conduct their own clinical trials, ANDAs require only that a generic manufacturer conduct studies to show that a proposed drug is pharmaceutically equivalent to the marketed drug, and meets a certain level of bioequivalence.[58] This new pathway reduces the amount of time for a generic manufacturer to bring a new drug into the market, typically when a brand name drug is nearing the expiration of its main compound patent. The newfound competition drastically increases the availability of medication within the market and

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[51] Shepherd, *supra* note 11, at 4.
[52] *Id.*
[53] *Id.*
[54] *Id.*
[55] *See, e.g.*, Sara Ponziani et al., *Antibody-Drug Conjugates: The New Frontier of Chemotherapy*, INT'L J. MOLECULAR SCI. (2020). The article discusses the novel use of antibody-drug conjugates ("ADCs"), which have become one of the most promising developments in cancer treatments. The ADCs selectively target antigens on tumor cells that are expressed at higher levels than normal cells. The treatments are often more effective in patients who exhibit higher levels of expression of certain cells, and results may vary significantly based on the presence of specific antigens. The changes in level in response have garnered the attention of numerous scientists and may lead to more "personalized medicine" in the future.
[56] Shepherd, *supra* note 11, at 4.
[57] *Role of Patents and Exclusivities*, *supra* note 27, at 13.
[58] *Id.*

reduces the cost of the drug to consumers—the profits of a patent owner will face a steep decline upon the entry of even the first competitor.[59]

While increasing availability of medicine to individuals, and subsequently reducing costs has become of paramount importance to many, federal law attempts to balance this interest with stimulating innovation.[60] In order to incentivize firms to undertake the arduous process of obtaining approval for a new drug, federal law provides regulatory exclusivity that "limits the FDA's ability to approve generic drugs and biosimilars . . ."[61] Commentators refer generally to two types of exclusivity: (1) data exclusivity, which "precludes other applicants from relying on the FDA's safety and effectiveness findings . . ." for a marketed product (i.e., clinical trial data), and (2) marketing exclusivity, which "precludes [the] FDA from approving any other application for the same pharmaceutical product and use . . .."[62] For an applicant who files a drug that contains a new chemical entity, meaning it contains a new active ingredient, data exclusivity will be awarded for "five years from the date of the approval of the application."[63] In the case of an NDA that contains an approved chemical entity, but is sufficiently changes from an approved drug, it is granted a period of "three years from the date of the approval of the application" for data exclusivity.[64] Finally, the Hatch-Waxman Act provides a 180-day exclusivity for the first generic manufacturer who successfully files an ANDA.[65]

II. INCENTIVES FOR CONSOLIDATION

A. Economists' Perspective

Economists have long theorized over the effect that competition among firms will have on innovation and the ways in which it will impact social welfare.[66] Two of the most prolific models from which antitrust authorities have modeled merger review guidelines were advanced by

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[59] Cooter & Hacohen, *supra* note 17, at 231–32.
[60] *Role of Patents and Exclusivities*, *supra* note 27, at 16.
[61] *Id.*
[62] *Id.*
[63] 21 U.S.C. § 355(c)(3)(E)(ii).
[64] *Id.* at § 355(c)(3)(E)(iii).
[65] 21 U.S.C. § 355(j)(5)(B)(iv). *See* Shepherd, *supra* note 11, at 9 (explaining that if a generic company can bring a drug to market during a period of 180-day exclusivity, in which no other generic competitors can market their drug, it will result in substantial profits).
[66] Majure et al., *supra* note 2, at 1.

Kenneth Arrow and Joseph Schumpeter.[67] Schumpeter espoused that concentrating resources between firms into oligopolies may actually promote innovation by creating market power and the ability to leverage economies of scale.[68] Arrow was critical of this approach and responded by noting that monopolistic behavior may stifle innovation.[69] Instead, he thought that competition among firms would incentivize companies to pursue further advances that a single firm would be unwilling to develop.[70] While there has been no general consensus among academics, economists have often noted confounding variables in examining the effects of competition on innovation.[71]

Carl Shapiro attempted to find compatibility between the competing theories in his chapter "Competition and Innovation: Did Arrow Hit the Bull's Eye."[72] He provides three guiding principles that may be utilized to examine innovation: (1) the contestability principle, (2) the appropriability principle, and (3) the synergies principle.[73] He defines contestability as "[t]he prospect of gaining or protecting profitable sales by providing greater value to customers," which would increase overall innovation.[74] By providing a more valuable product to consumers, examined based on the nature of ex post product market competition, a firm would be more likely to capture profits from the endeavor.[75] Appropriability "focuses on the extent to which a successful innovator can capture the social benefits resulting from its innovation."[76] In practice, appropriability requires that a firm be able to exploit its competitive advantage, and differentiate its profits from competitors.[77] Finally, the synergies principle explains that "[c]ombining complementary assets enhances innovation capabilities and thus spurs innovation."[78] Shapiro notes that the synergies resulting from business combinations is uniquely important in industries where value is derived from systems that incorporate multiple components—downstream innovation may require previous knowledge or technology to build upon

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[67] Polydorou et al., *supra* note 3, at 70.
[68] *Id.*
[69] *Id.*
[70] *Id.*
[71] Majure et al, *supra* note 2, at 1.
[72] Carl Shapiro, *Competition and Innovation: Did Arrow Hit the Bull's Eye*, THE RATE AND DIRECTION OF INVENTIVE ACTIVITY REVISITED, 361–404 (Josh Lerner & Scott Stern eds., 2012).
[73] *Id.* at 364–65.
[74] *Id.* at 364.
[75] *Id.*
[76] *Id.*
[77] *Id.*
[78] *Id.* at 365.

prior work.[79] While contestability and appropriability offer *incentive* to innovate, synergies focuses on a firm's *ability* to innovate.[80]

B. Competition in the Pharmaceutical Industry

Over the past two decades, the pharmaceutical industry has produced groundbreaking new medicines that have fundamentally changed the way that society treats illnesses that have crippled the lives of individuals for centuries. Promising advances in immunotherapy provide courses of treatment for patients suffering from cancer[81] and novel vaccines allow a barrier of protection against COVID-19.[82] Given the rapid advancement in science and massive shifts in R&D efforts to produce new drugs, the expectation would be for new companies to emerge as frontrunners in the industry, backed by large profits stemming from their innovation. In the opposite fashion, the pharmaceutical industry has been shaped by the persistence of the same list of large firms over the years.[83] In fact, the top 20 pharmaceutical firms of 2009 are remarkably similar to the top 20 firms in 2019, with only a few new companies emerging as powerhouses in the industry.[84] Explaining the continued dominance of a few firms is the "extensive, industry-wide pattern of acquisition" as large firms seeks to enhance their product pipeline and R&D that supplement a lack of organic development.[85]

Examining this phenomenon using Shapiro's framework, it is clear that all three of his stated principles are acting in the market. For contestability, when a popular new drug is introduced to the public, the demand for life-saving treatment will be overwhelming. Consider two drugs: Drug A and Drug B. Drug A is remarkably effective at treating a disease and produces little to no side effects within patients. Conversely,

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[79] *Id.*
[80] *Id.*
[81] *See, e.g.*, Sofia Farkona et al., *Cancer Immunotherapy: The Beginning of the End of Cancer?*, 14 BMC MED. (2016). Scientists have long sought to exploit the human immune system as a means of treating tumors and malignant cells. Through the discovery of specific antibodies, current research focuses on targeting antibodies with immune cells to either stimulate or inhibit immune responses in the body. In combination with other therapies, immunotherapy has become increasingly effective in treating various forms of cancer, including melanoma.
[82] *See Decades in the Making*: *mRNA COVID-19 Vaccines*, NAT'L INST. HEALTH (last visited Jan. 7, 2023) for a discussion on the development of mRNA vaccines. FDA-approved mRNA vaccines have been essential in saving millions of lives during the COVID-19 pandemic and may be further researched for application to other illnesses.
[83] Danzon & Carrier, *supra* note 15, at 493.
[84] *Id.* at 493–94.
[85] *Id.* at 495.

Drug B is a similar treatment for a given disease, but clinical trials show less efficacy and countless negative side effects. When given open competition on the market, rational doctors and patients will choose Drug A on every occasion, leading to a wave of sales derived from the inherent value of the drug, and it will likely become a blockbuster treatment for a pharmaceutical company. While in the ideal world, firm profits will reflect the value to consumers, it is evident that this will not always be the case because companies still have to satisfy the principle of appropriability. In order to profit from Drug A, a company will have to successfully obtain patent protection for its invention, meet all of the stringent criteria for FDA approval including clinical trials, and will only be able to exploit its protection for a period of 20 years (often less after navigating the process of regulatory approval). Even if a small firm were able to produce the next miracle treatment, it is unlikely that it would be able to capture profits from its invention by navigating through the unwieldy and costly process. Given the average cost of developing a new drug is estimated at $2 billion,[86] the hurdles eliminate competition from the vast majority of firms in the market, even before the entry of generic manufacturers.

Next, consider a scenario where Drug A provides benefits beyond just its use for treatment of a single indication. Instead, it provides a mechanism of action that other researchers can base their own novel drugs off, leading to a "series of possible discoveries."[87] Introducing this complication into the hypothetical dilutes the current appropriability of a single breakthrough, as subsequent discoveries become more profitable and leaving the original discovery obsolete. Instead, profits are most efficiently realized through synergy between firms, as researchers collaborate to produce the most effective treatment possible. Cooter and Hacohen describe this effect as the "fertility principle:" an innovation that "can be used to create another innovation."[88] Given the complexity associated with the development of pharmaceuticals and the need for prior innovations to lead to downstream development, it seems more appropriate to focus on "increased human welfare" writ large, rather than on market power of a specific firm.[89]

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[86] *Research and Development in the Pharmaceutical Industry*, *supra* note 8, at 2.
[87] Majure et al., *supra* note 2, at 1.
[88] Cooter & Hacohen, *supra* note 17, at 205–06.
[89] *See id.* at 208–10.

C. Pathways to Innovation

While smaller startup companies, such as biotechnology firms, suffer from an inability to compete with incumbent firms to bring new drugs to market, they act as a primary source of R&D in the pharmaceutical industry.[90] In fact, internal R&D has been completely overtaken in the market as "three-fourths of new drugs are externally-sourced."[91] While traditional pharmaceutical companies have often focused on synthetic chemical entities, consisting mostly of small molecules, biotech companies focus on applying elements of living cells to new treatments (e.g., antibodies that target specific antigens).[92] Larger incumbent firms offer a pathway to bring new drugs to market as they "devote significant efforts to [] clinical testing, marketing, manufacturing, and distribution of drugs.[93] Given the increasing importance of smaller firms in the market, it becomes important to define the "current drug innovation ecosystem," in which larger firms must seek acquisitions, joint ventures, and licenses in order to continue their drug development pipelines.[94]

In her article, Shepherd describes four attributes that give biotech companies a comparative advantage over large pharmaceutical companies in early-stage drug development.[95] First, she notes that startup companies typically operate on a much smaller scale when conducting R&D and developing new treatments.[96] The small organizational structure gives the firm the important flexibility needed to pursue risks that may be unsuccessful, and could not be considered at a larger firm due to their need to act in the best interests of shareholders.[97] Second, biotech companies enjoy close partnerships with nonprofit research institutions, where some of the country's leading scientists can pursue academic research without the worry of commercialization.[98] Additionally, the Bayh-Doyle Act of 1980 allows non-government entities to apply for patents resulting from programs that receive federal funding.[99] Third, due to their significant risk, but

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[90] Shepherd, *supra* note 11, at 2.
[91] *Id.*
[92] *Id.* at 17.
[93] *Id.*
[94] *Id.* at 16–18.
[95] *Id.* at 21–23.
[96] *Id.* at 21.
[97] *Id.*
[98] *Id.*
[99] *Id.* at 18. *See* 35 U.S.C. § 202(a) (allowing nonprofit organizations or small businesses to "elect to retain title to any subject invention").

potentially substantial upside, biotech firms often receive their funding from venture capitalists ("VCs") or private equity firms.[100] While the steady stream of capital allows smaller firms to pursue goals that would otherwise be unattainable, many VCs push the ventures toward an exit from the market, either through sale of the company or licensure of the invention.[101] Finally, the culture of creativity and innovation, coupled with significantly less bureaucratic oversight, attracts some of the nation's brightest researchers to smaller companies.[102] Indeed, when discussing killer acquisitions, Cunningham et al. considered that large pharmaceutical companies may acquire smaller firms in order to benefit from the human capital.[103] Interestingly, their data supports the proposition that only a relatively small number of researchers stay at the acquiring firm post-acquisition, reflecting the interest in remaining at smaller, more flexible companies.[104]

D. Issues for Large Pharmaceutical Companies

While acquisition can provide significant benefits for smaller startups, it has become critical for large firms to continue their commercial success. Higgins and Rodriguez postulated that M&A is most likely to occur in large pharmaceutical companies that have exhibited "deteriorating R&D productivity," especially when companies consider acquiring research-intensive firms.[105] They outline numerous options considered by pharmaceutical companies facing declines in productivity: (1) supplement internal R&D efforts through acquisition of smaller companies, (2) engage in large horizontal mergers to achieve greater economies of scale (3) acquire mature existing products through licensing agreements, (4) attempt to increase internal R&D efforts

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[100] Shepherd, *supra* note 11, at 22.
[101] For a full discussion on the motivations of VCs to force startup companies to sell to larger firms, *see generally* Mark A. Lemley & Andrew McCreary, *Exit Strategy*, 101 B.U. L. REV. 1 (2020). Similar to the pharmaceutical industry, technology companies in Silicon Valley face the pressures of accepting money from VCs who seek large returns on their initial investment. The article proposes changing incentives to maximize the number of startups that continue operations, finding different sources of funding for projects to relieve pressures, and providing regulatory responses that deter such action. While there are fundamental differences between the types of investment in small pharmaceutical companies and technology platforms, there is significant overlap and lessons to be learned from examining the nature of capital being infused in the firms.
[102] Shepherd, *supra* note 11, at 22.
[103] Cunningham et al., *supra* note 14, at 5.
[104] *Id.*
[105] Higgins & Rodriguez, *supra* note 18, at 352.

organically, (5) increase activity through alliances, or (6) change their fundamental business model.[106] In determining what type of acquisition may be the most advantageous for pipeline development, pharmaceutical companies face a significant challenge in information asymmetry—given the early stages of product development, it is often impossible to predict which research projects will be successful or result in overlap with existing products within a portfolio.[107]

One measure frequently used by both investors and academics as a proxy for real value in a pharmaceutical company is by looking at the number of successful patents that a company owns.[108] Given the tendency of pharmaceutical companies to deter patent infringement through a plethora of patents for features other than a new compound, it is often an unreliable measure of the actual value of a pharmaceutical company.[109] Instead of using a discrete number of patents as an index, subsequent studies instead used patent citations as indicative of social value, theorizing that highly-cited patents were more impactful on the industry, and would be used as prior art in subsequent patent applications.[110] While a patent-citation index may provide a useful approximation for those seeking to evaluate the patent portfolio of a company, the data is often based only on published materials, such as the FDA Orange Book[111] or the USPTO website.[112]

III. M&A IN THE PHARMACEUTICAL INDUSTRY

A. Merger Review

Blockbuster pharmaceutical acquisitions have become the norm within the industry, as large firms frequently engage in horizontal

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[106] *Id.* at 354.
[107] *Id.* at 356.
[108] *See* Polydorou et al., *supra* note 3, at 75.
[109] *See* DAVID S. ABRAMS & BHAVEN N. SAMPAT, PHARMACEUTICAL PATENT CITATIONS AND REAL VALUE, 1–3 (2017).
[110] *See id.* at 3.
[111] *See Approved Drug Products with Therapeutic Equivalence Evaluations | Orange Book*, FDA, https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book (last visited Mar. 5, 2023). The publication, commonly known as the "Orange Book" provides a comprehensive list of drug products approved by the FDA and related patent and exclusivity information. This database is a useful starting point, but does not include those drugs that have not received approval from the FDA and does not include information about biologic products.
[112] *See* Abrams & Sampat, *supra* note 109, at 4.

mergers to maintain their dominance.[113] The advent of the twenty-first century saw massive deals from Pfizer, Merck, Bristol-Myers Squibb ("BMS"), and AbbVie, each to acquire leading products on the market that produced massive profits through global sales.[114] Following the massive influx of revenue from sales of COVID-19 vaccines and other anti-viral drugs, pharmaceutical companies have continued to seek new companies to expand upon their existing product pipeline.[115] As larger incumbent firms continue to swallow smaller startup companies, academics and regulators have become increasingly concerned with the anticompetitive nature of the transactions, especially when existing products overlap with those in the target company.[116] Interestingly, despite broader concerns about consolidation in the pharmaceutical industry and rising prices, essentially no transaction has been blocked by the FTC.[117] According to a study by the American Antirust Institute from 1994 to 2020, the FTC "challenged 67 pharmaceutical mergers worth over $900 billion, moved to block only one, and settled virtually all the remainder subject to divestitures."[118]

While M&A can provide positive social benefits, the FTC recognizes that "[s]ome mergers change market dynamics in ways that can lead to higher prices, fewer or lower-quality goods or services, or less innovation."[119] Under traditional merger review, M&A is prohibited under section 7 of the Clayton Act when it "substantially lessen[s] competition or tend[s] to create a monopoly."[120] Combinations of all types can cause harm to consumers, but the largest antitrust concerns arise when mergers are proposed between direct competitors in the same

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[113] Danzon & Carrier, *supra* note 15, at 493.
[114] *Id.* For example, Pfizer acquired Warner-Lambert to obtain Lipitor, and upon its patent expiration, acquired Wyeth to add Prevnar to its portfolio. Merck acquired Schering-Plough and benefited from an unexpected blockbuster cancer treatment in Keytruda. *Id.*
[115] *See, e.g.*, Rebecca Robbins & Peter S. Goodman, *Pfizer Reaps Hundreds of Millions in Profits from Covid Vaccine,* NY TIMES (May 5, 2022), https://www.nytimes.com/2021/05/04/business/pfizer-covid-vaccine-profits.html; George Budwell, *Biopharma's 5 Biggest M&A Deals of 2022*, BIOSPACE (Dec. 23, 2022), https://www.biospace.com/article/biopharma-s-5-biggest-m-and-a-deals-of-2022/.
[116] *See* Polydorou et al., *supra* note 3, at 71–73.
[117] *See* Danzon & Carrier, *supra* note 15, at 488–89.
[118] *Id.* at 489 (quoting Diana L. Moss*, From Competition to Conspiracy: Assessing the Federal Trade Commission's Merger Policy in the Pharmaceutical Sector 10,* AM. ANTITRUST INST. (Sept. 3, 2020)).
[119] *Mergers, Guide to Antitrust Laws*, FTC, https://www.ftc.gov/advice-guidance/competition-guidance/guide-antitrust-laws/mergers (last visited Jan. 8, 2023).
[120] 15 U.S.C. § 14.

industry.[121] Additionally, the Hart-Scott-Rodino Antitrust Improvements Act of 1976 imposed a pre-merger notification requirement to both the DOJ Antitrust Division and the FTC when the proposed transaction exceeds $200 million.[122] As a result, the pre-merger notice allows regulators to challenge mergers before they are consummated, often resulting in abandonment or divestiture, while those that fall below the dollar threshold are not subject to scrutiny.[123]

While competition authorities have varied in their approaches to considerations of harm in pharmaceutical mergers, the traditional practice was "almost exclusively concerned . . . with existing products, or those contemplated in the merging firms' pipelines."[124] This understanding acknowledges the fact that mergers may increase innovation by providing changes in investment incentives—such as shared intellectual property between firms about knowledge of disease targets, or by implementing next generation or lower cost technologies—and thus there should be a "neutral rather than negative presumption . . . for merger innovation efforts."[125] In the United States, the FTC historically focused on Phase III pipeline products when considering remedies (e.g., divestiture), but has also considered products in the FDA pipeline, including those in the pre-clinical stages.[126] While the FTC has often been unwilling to challenge pharmaceutical mergers, in recent years a number of commissioners have notably dissented from the majority calling for further innovation activism.[127] In his dissenting statement in *AbbVie/Allergan*, Commissioner Rohit Chopra issued a grave warning, stating that "[t]he agency's default strategy of requiring merging parties to divest overlapping drugs is narrow, flawed, and ineffective."[128] It allows "pharmaceutical companies to further exploit

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[121] *Mergers, supra* note 119; *see also* Danzon & Carrier, *supra* note 15, at 490 (discussing how a merger of two large firms in the pharmaceutical sector negatively impacts the industry by harming competitors and consumers, reducing incentives to innovate, and entrenching the acquiring firms position in the market).
[122] 15 U.S.C. §§ 18(a)–(b).
[123] Amy C. Madl, *Killing Innovation? Antitrust Implications of Killer Acquisitions*, 38 YALE J. ON REG. BULL. 28, 40 (2020).
[124] Polydorou et al., *supra* note 3, at 70.
[125] *Id.* at 72.
[126] *Id.* (explaining the current state of the FTC approach to innovation in pharmaceutical mergers). In contrast, the EC has codified a four-level approach, examining: (1) overlaps between existing products; (2) overlaps between existing and pipeline products, and between pipeline products and those in advanced stages of development; (3) loss of innovation competition resulting from changes in pipeline products with existing products; and (4) loss of innovation competition resulting from a structural reduction of the overall level of innovation. *See id.* at 73.
[127] *Id.*
[128] Dissenting Statement of Commissioner Rohit Chopra at 2, AbbVie, Inc./Allergan

their dominance, block new entrants, and harm patients in need of life-saving drugs."[129]

B. Innovation as a Theory of Harm

Given the increasing concern with M&A activity in the pharmaceutical industry, leading antitrust enforcers across Europe and North America have banded together to assess the "full range of a pharmaceutical merger's effects on innovation[.]"[130] While other industries may follow a deterministic process with discrete inputs and observable outputs, it is seemingly impossible to derive the value of future innovation from early-stage developments.[131] In their article, Majure et al. discuss the complications in observing effects on innovation stemming from evidence and measurement.[132] First, attempts to provide a singular model for examining mergers may be ineffective because innovation is not a homogenous subject.[133] Instead, a transaction may harm consumers by producing fewer cost-reducing technologies, raise prices, or a firm may abandon plans to develop future products.[134] In order to appropriately quantify changes in the level of future innovation, experts must provide a specific model for each characteristic, backed with empirical evidence focusing on that attribute.[135] Second, changes in innovation within pharmaceutical companies do not directly correspond to changes in social welfare as directly as other factors (e.g., prices).[136]

Aside from the difficulty in choosing an accurate model, it is equally problematic to find appropriate metrics from which regulators can determine what type of activity would be anticompetitive. Polydorou et al. explain that authorities have previously used both past product launches and patent citation indexes as measures of innovation

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plc, FTC File No. 191-0169 (May 5, 2020).

[129] *Id.*

[130] Polydorou et al., *supra* note 3, at 71.

[131] *See* Majure et al., *supra* note 15, at 1.

[132] *Id.* at 2.

[133] *Id.*

[134] *Id.*

[135] *Id.*

[136] *Id.*; *see also* Shepherd, *supra* note 11, at 6–28. Professor Shepherd argues that in the current drug innovation ecosystem, M&A will not stifle innovation. Since most R&D occurs outside the purview of large pharmaceutical companies, it is "largely missing the point" to focus on organic R&D efforts. In addition, social welfare is more directly impacted by other critical factors, such as competition from generic manufacturers, pharmacy benefit managers who administer prescription drug coverage for Americans with health insurance, and the costs associated of compliance with FDA guidelines.

potential.[137] While some correlation may exist, it is difficult to examine backward-looking measures for future innovation, as pharmaceutical companies often acquire nascent or early-stage pipeline products.[138] In these cases, past product launches and patent citations would not accurately reflect the impact on future product development.[139] Another measure that has been considered is outsized valuations, meaning that a high deal value may be suspect, giving the impression that the acquiring company overpaid in order to hinder competition.[140] However, attempting to determine the motive of executives and business development teams is a fruitless endeavor, as there are numerous justifications for acquisitions that are considered a "rational business decision."[141] Finally, regulators often turn to internal communications as evidence of innovative intentions.[142] However, this again may be misleading, as the authors note that "[d]ocuments may be created by people without the necessary knowledge or authority to implement the ideas they contain, may represent early thinking that was quickly rejected, or may have been created to 'sell' a certain view of the world to a specific audience."[143]

C. Killer Acquisitions?

In their frequently cited paper *Killer Acquisitions*, Cunningham et al. discuss the possibility that drugs acquired through acquisition are less likely to be developed when they overlap with an existing product in the acquirer's portfolio.[144] Citing Arrow, the authors hypothesize that an incumbent acquirer will have reduced incentives to continue a project if it directly competes with, or substitutes for, an existing project.[145] To qualify as an "overlapping acquisition," a competing product must be in the same therapeutic class (i.e., used to treat a particular disease) and must use the same mechanism of action to treat the patient (i.e., how the drug is delivered).[146] The paper suggests three main objectives from the

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[137] Polydorou et al., *supra* note 3, at 74–75.
[138] *Id.*
[139] *Id.*
[140] *Id.* at 75.
[141] Madl, *supra* note 123, at 31.
[142] Polydorou et al., *supra* note 3, at 75.
[143] *Id.*
[144] Cunningham et al., *supra* note 14, at 650.
[145] *Id.* at 651 (citing Kenneth Arrow, *Economic Welfare and the Allocation of Resources for Invention*, *in* THE RATE AND DIRECTION OF INVENTIVE ACTIVITY: ECONOMIC AND SOCIAL FACTORS 609, 622 (Princeton Univ. Press, 1962)).
[146] *Id.* at 652.

research: (1) to highlight that killer acquisitions are a fundamental impediment to corporate innovation, as firms seek to protect existing profits; (2) the effect of such acquisitions on innovation in the pharmaceutical industry, where future discoveries have a crucial link to social welfare; and (3) that this trend leads to consolidation of firms within the industry, as incumbents reduce competition by acquiring nascent companies to deter future competition.[147] According to the empirical data, acquisitions motivated by efforts to hinder the development of overlapping products occur at an estimated rate of approximately 7 percent per year.[148]

While Cunningham et al. come to the conclusion that killer acquisitions will have a negative effect on consumer surplus, both through decreasing the number of drugs sold and increased prices,[149] they recognize that there may be alternative explanations for the trend.[150] Importantly, the authors discuss optimal project selection as a motivation behind terminating future development of a product post-acquisition, although they remain skeptical of its importance.[151] The brief discussion neglects to consider that the majority of acquisitions that take place are of smaller biotechnology companies, whose product pipelines include many promising drug candidates at varying stages of clinical development. An acquiring firm, similar to other investors, takes a gamble on numerous drugs with the hope that a small number of those products will be a commercial success, or a "blockbuster" drug.[152] Furthermore, an acquiring firm may gain invaluable *negative* information about specific drug candidates or mechanisms of action that lack functionality.[153] Finally, Cunningham et al. explain that acquiring companies do not redeploy drugs in their own internal projects post-acquisition, finding that future projects largely do not share chemical similarities to drugs acquired from the target.[154] While the authors use a period of five years after the acquisition date in order to observe

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[147] *Id.* at 655.
[148] *Id.* at 692.
[149] *Id.* at 694.
[150] *Id.* at 687–91. The paper focuses five alternative explanations for the phenomenon: (1) informational asymmetries in the acquisition market, (2) optimal project selection, (3) redeployment of technologies, (4) redeployment of human capital, and (5) salvage acquisitions. While recognizing varying incentives among acquiring firms, the authors explain that it is unlikely these play a substantial role in practice. *Id.*
[151] Cunningham et al., *supra* note 14, at 688.
[152] *See* Shepherd, *supra* note 11, at 22–25 (explaining that acquisition, licensing, and collaboration with biotech companies allow large pharmaceutical companies to develop specialized medicines).
[153] Madl, *supra* note 123, at 38.
[154] Cunningham et al., *supra* note 14, at 688.

similarities in molecular structure, this notably fails to account for the fact that the development process often "take[s] a decade or more."[155] Increasingly, pharmaceutical companies have sought to take advantage of initial breakthroughs by employing combination therapies, often finding new indications that benefit from similar courses of treatment.[156]

IV. INCREASING DOWNSTREAM INNOVATION

While increasing scrutiny on M&A in the pharmaceutical industry may lead to fewer consummated transactions and lower costs for consumers in some cases, it will also have the unwanted effect of reducing total consumer surplus as investors shy away from infusing capital into drug development. Allowing companies to set prices at levels that exceed the cost of manufacturing yields profit and higher profits increase the incentive to innovate.[157] While there is certainly a tradeoff between access to healthcare and incentives to innovate, society will benefit when the rate of innovation exceeds any losses from inefficiency in the market (e.g., discontinuation of certain products).[158] Instead of focusing on the acquisitions of products in the development pipeline—an essential element of the structure of the current innovative ecosystem[159]—government authorities should reduce barriers to innovation by expanding exemptions from patent infringement for follow-on research.

A. Justifications for Exemptions from Patent Infringement

According to the Constitution, Congress is authorized to make patent law to "promote the Progress of Science and useful Arts."[160] According to Cooter and Hacohen, lawmakers can only fulfill this constitutional purpose by effecting *progress*, measured by the increased quality of life of individuals in the aggregate.[161] Bearing on economic principles, the pair defines two fundamental precepts of patent law

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[155] CONG. BUDGET OFF., *supra* note 8, at 5.
[156] *See, e.g.*, Reza Bayat Mokhtari et al., *Combination Therapy in Combating Cancer*, 8 ONCOTARGET 38022, 38022 (2017), https://pubmed.ncbi.nlm.nih.gov/28410237/ (discussing combination therapy, a method of treatment that combines two or more therapeutic agents, as increasing efficacy in the treatment of certain cancers).
[157] Cooter & Hacohen, *supra* note 17, at 196.
[158] *See id.*
[159] Shepherd, *supra* note 11, at 16–25.
[160] U.S. CONST. art. I, § 8, cl. 8.
[161] *See* Cooter & Hacohen, *supra* note 17, at 193.

policy: the "separation principle" and the "overtaking principle."[162] First, the separation principle denotes that patent protection should be "strong against using an innovation to consume or produce, and weak against using an innovation to innovate."[163] A patent serves the purpose of allowing its inventor to reap profits from their innovation; when a consumer purchases that invention, wealth is transferred from the individual to the inventor, providing incentives for reinvestment and future innovation.[164] Conversely, when the innovation is used by a subsequent inventor to produce their own innovation, wealth is transferred between two parties both seeking to provide novel inventions, likely reducing overall consumer surplus through deadweight loss and inefficiency in the form of transaction costs.[165] Second, the overtaking principle explains that the welfare gains from the exponential growth stemming from innovation will outweigh any losses from static inefficiencies in the market.[166] Therefore, "in the absence of aggravating circumstances, escalated consumer products' prices should not justify reform" within the traditional structure of exclusivity for innovators.[167]

In a recent article, Professor Janet Freilich outlines that, due to the sequential nature of discovery, the patent system may provide a fundamental roadblock to downstream innovation, as future experimentation often falls within the scope of an upstream patent.[168] In some cases, scientists "cannot conduct even the most basic research towards downstream technologies without addressing the upstream patent."[169] The structure of the patent system leaves open three possibilities: (1) the innovator licenses the upstream patent (which can have the negative effect of notifying other researchers about future intentions); (2) the party infringes a blocking patent; or (3) research is done outside the scope of an existing patent, which is not defined as patent infringement.[170] While other scholarship has reflected the viewpoint that these possibilities hinder research from taking place, Professor Freilich explains it instead provides incentives for research to take place in areas that are exempt from patent infringement.[171] While

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[162] *Id.* at 195–97.
[163] *Id.* at 195.
[164] *Id.*
[165] *Id.*
[166] *Id.* at 196.
[167] *See id.*
[168] Janet Freilich, *Paths to Downstream Innovation*, 55 U.C. DAVIS. L. REV. 2209, 2211–12 (2022).
[169] *Id.* at 2209.
[170] *Id.* at 2212.
[171] *Id.*

patents do not provide "a near-total block" to future innovation, they "pull downstream research along haphazard and arbitrary paths."[172] Instead of incentivizing discrepancies between different research projects, regulators should reshape the patent system to ensure that society is taking advantage of all future innovation to increase human welfare.

B. Common Law Research Exemption

Justice Story famously advanced the theory that using patented technology to experiment should not be included within the scope of patent infringement, which has provided a basis for research exemptions in the common law.[173] He argued that "it could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."[174] While there has been little Congressional action to address a basic scientific research exemption from patent infringement, subsequent case law has confirmed that such a principle exists.[175] In *Poppenhusen v. Falke*, the court stated that "an experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement is not an infringement of the rights of the patentee."[176] The common law research exemption has slowly been eroded over the years, culminating in a decision from the Federal Circuit in *Madey v. Duke University*.[177] There, the court determined that experiments conducted by the research institution using a patented laser did not qualify for the experimental use defense, as the projects "unmistakably further[ed] the institution's legitimate business objectives."[178] Duke University had conducted the experiments with the goal of gaining notoriety, which the court proposed could be used to obtain federal grants and was used in recruiting both faculty and students.[179]

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[172] *Id.*
[173] *See* Whittemore v. Cutter, 29 F. Cas. 1120, 1120–23 (C.C.D. Mass. 1813).
[174] *Id.* at 1121.
[175] Jorge A. Goldstein, *The Law on Research Exceptions – Common Law Exceptions*, U.S. BIOTECHNOLOGY PAT. L. § 12:35 (2022).
[176] *Id.* (quoting Poppenhusen v. Falke, 19 F. Cas. 1048, 1049 (C.C.S.D. N.Y. 1861)).
[177] Madey v. Duke University, 307 F.3d 1351 (Fed. Cir. 2002).
[178] *Id.* at 1362.
[179] *Id.*

C. Other Exceptions to Infringement

Professor Freilich discusses numerous other ways that research may fall outside the scope of patent infringement, and how arbitrary lines provide differing incentives for downstream innovation.[180] In the context of pharmaceuticals, one of the other most important exemptions from patent infringement is a safe harbor provided by Congress, known commonly as a "Bolar Exception." In response to the ruling in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*,[181] Congress included a provision in the Hatch-Waxman Act that exempted experimental use from patent infringement when the relevant research was used to obtain approval by the FDA prior to marketing.[182] The statute states that "[i]t shall not be an act of infringement to make, use, offer to sell, or sell . . . a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs . . ."[183] While many assumed that the statutory safe harbor was meant exclusively for generic drug manufacturers in order to obtain regulatory approval before the expiration of a patent, the Supreme Court repudiated this view.[184] The Court explained that Congress did not limit the exemption to developing information for submission to the FDA in the process of generic drug approval—"it exempted from infringement *all* uses of patented compounds 'reasonably related' to the process of developing information for submission under *any* federal law regulating the manufacture, use, or distribution of drugs."[185]

The practical effect of the safe harbor provided under section 271(e)(1) is that large swaths of life sciences research is exempted from patent infringement, including preclinical studies and other testing on drugs that is "reasonably related" to regulatory approval.[186] However, the

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[180] *See* Freilich, *supra* note 168, at 2225–50. The article gives a full discussion of downstream research that is considered "not infringement" and compares such activity to things that qualify as "infringement." Importantly, she highlights specific areas of research that can produce innovation without infringing on a patent owners exclusivity, including (1) new methods of using an existing product, (2) research on commercially available products, (3) late-stage life sciences research, (4) research at state universities, (5) research outside the jurisdiction of the United States, (5) thinking about hypotheses, (6) secret research, (7) low-cost research, and (8) research in areas where patent rights are not voluntarily enforced. *Id.*

[181] Roche Prod., Inc. v. Bolar Pharm. Co., 733 F.2d 858 (Fed. Cir. 1984).

[182] 35 U.S.C.A. § 271(e)(1) (Westlaw through Pub. L. No. 111—148).

[183] *Id.*

[184] *See* Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 206 (2005).

[185] *Id.* (Emphasis included).

[186] Freilich, *supra* note 168, at 2231.

exception does not cover all downstream research in the pharmaceutical sector, such as basic scientific research, where a clinical candidate has not yet been selected.[187] Additionally, the safe harbor has not been expanded to areas where regulatory approval by the FDA or other agencies is not required, leaving out advances in adjacent fields that may provide technological innovation that can reduce the costs to develop certain drugs.[188]

D. Reduced Cost to Innovate Increases Social Welfare

While pharmaceutical M&A may have anticompetitive effects on the market, the difficulties in quantifying which transactions qualify, the costs associated with enforcement, and the reduced incentives to innovate, make merger review an inefficient method of addressing costs to consumers. Instead, regulatory authorities should focus on reducing hurdles to competition through patent further exemptions to patent infringement, and encouragement of collaboration between parties that have little to no desire to commercialize products. The Bolar Exception under Section 271(e)(1) provides a method for generic competition to enter the market sooner, effectively reducing the prices of brand name drugs earlier in their life cycle. Moreover, private, non-profit research institutions should be protected in conducting groundbreaking research, so long as there are no extenuating circumstances that make clear the primary goal is commercialization. Partnerships between research institutions and small startup companies have proven exceptionally successful and provide glamorous targets for acquisition and development by large companies.[189]

CONCLUSION

The COVID-19 pandemic highlighted the importance of cooperation between the pharmaceutical industry, healthcare providers, and government officials. Barriers to access can leave individuals without life-saving treatments that can be a determinative factor in whether that

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[187] *Id.* at 2232.
[188] *Id.*
[189] *See, e.g.*, Heather McKenzie, *Merck's Molnupiravir: When a Private-Public Partnership Bears Fruit*, BIOSPACE (Nov. 3, 2022), https://www.biospace.com/article/merck-s-molnupiravir-when-a-private-public-partnership-bears-fruit-/ (examining the successful partnership between Merck, Emory University, and Ridgeback Biotherapeutics in producing a "miracle drug" used to treat COVID-19).

person lives or dies. Highlighted by media stories and quick jabs from politicians, large pharmaceutical companies have carried much of the blame for inefficiencies in the prescription drug market and increasing prices that effectively limit lower-income individuals from receiving the care they need. While increasing scrutiny from antitrust authorities may provide a feasible solution to the problem, it will only increase the costs for M&A to occur in the pharmaceutical industry. Likely, these costs will be passed onto consumers, or reduce the incentive for innovation of future miracle treatments. It is nearly impossible to delineate ascertainable metrics to use in merger review, and thus innovation as a standalone theory of harm will prove too difficult for regulators to practically enforce.

While the current innovation ecosystem—where smaller startup and biotechnology firms, backed by venture capitalists, are acquired by larger incumbent firms—may leave many uneasy, it is a necessary evil to allow continued growth in the area. Specialization within in smaller firms allows treatment for rare diseases and small populations, who may otherwise be left without any treatment. Policymakers should instead focus on ways to encourage collaboration and innovation partnerships, through expanding exemptions to patent infringement. Given the limited term of patent protection, executives in pharmaceutical companies recognize that the only way to maintain success is by developing a robust product pipeline. In a world where M&A is the primary source of development for incumbent firms, the focus should be on providing resources to startup companies and non-profit research institutions, with the hope that the next breakthrough idea will be acquired and commercialized by a large company. While the current patent system may not provide the ideal solution for intellectual property protection, there are avenues to increase social welfare dramatically.