COMPETING WITH PATENT THICKETS: ANTITRUST LAW'S ROLE IN PROMOTING BIOSIMILARS

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ABSTRACT

Biologics, a new class of large-molecule drugs, have revolutionized the healthcare industry, offering powerful treatments to previously untreatable diseases. However, the complex science required to create a biologic results in extremely high development costs, which translates into expensive drug prices. In an effort to combat these high prices, Congress implemented a regulatory framework to allow competing companies to create generic versions of biologics, called biosimilars. Despite this framework, very few biosimilars have entered the U.S. market. Why? One major roadblock is the patents the original biologic manufacturer obtains to protect its drug. Because of the complexity of biologics, companies can create patent thickets, dense webs of overlapping patents on the drug and the processes for creating it. This huge volume of patents can obscure the scope of what the company owns and what a hopeful biosimilar manufacturer can do without facing patent litigation. These thickets can also extend the period during which the original manufacturer can exclusively market the drug.

Because of the high development costs associated with biologic and biosimilar development, few companies have the resources to enter the space. Patent thickets further limit competition for the original biologic, resulting in high drug prices for patients years after the original patents expire. After explaining why the scientific constraints and regulatory environment already make biosimilar manufacturing a difficult process, this Note explores how biologic companies create patent thickets and wield them to threaten biosimilar manufacturers, sometimes forcing them into collusive settlement agreements. Finally, this Note argues that the formation and anticompetitive use of patent thickets to prevent biosimilar competition should warrant antitrust sanction.

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INTRODUCTION

On December 31, 2002, the Food and Drug Administration ("FDA") approved adalimumab, marketed under the brand name Humira, a revolutionary new treatment for rheumatoid arthritis.[1] Humira was revolutionary not only for its effectiveness in the treatment of this autoimmune disease[2] but also for its broader advancement of the science in fighting disease: Humira was the first FDA-approved humanized monoclonal antibody,[3] part of a new class of large-molecule drugs known as biologics.[4] Humira demonstrated the power of this new technology: instead of inhibiting the immune system broadly like earlier therapies,[5] Humira targets a single molecule,[6] resulting in faster symptom relief.[7] Targeting this specific molecule proved effective in numerous other autoimmune diseases, leading the FDA to approve Humira for the treatment of twelve separate diseases.[8] Patients quickly flocked to Humira—50,000 patients

[1] *FDA Approves Humira*, DRUGS.COM, https://www.drugs.com/newdrugs/fda-approves-humira-adalimumab-rheumatoid-arthritis-77.html [https://perma.cc/F9BV-F446] (last visited Jan. 30, 2022).

[2] *Id.* (describing clinical data supporting FDA approval, including "an improvement in [rheumatoid arthritis] signs and symptoms as early as one week" and noting some durable responses lasting up to three years).

[3] Valderílio Feijó Azevedo, Ludmila Della Coletta Troiano, Natalia Bassalobre Galli, Alais Kleinfelder, Nathan M. Catolino & Paulo Cesar Urbano Martins, *Adalimumab: A Review of the Reference Product and Biosimilars*, 6 BIOSIMILARS 29, 30 (2016).

[4] *What Are "Biologics" Questions and Answers*, FDA, https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers [https://perma.cc/76UL-XD9K] (last updated Feb. 6, 2018) ("Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins.").

[5] Debra Fulghum Bruce & Alyssa Etier, *The Consumer's Guide to Biologics for Psoriasis*, EVERYDAY HEALTH, https://www.everydayhealth.com/psoriasis/the-consumers-guide-to-biologics-for-psoriasis/ [https://perma.cc/VD7F-GR2F] (last updated Feb. 24, 2021) (noting that nonbiologic medications for psoriasis, an autoimmune disease, "broadly suppress the immune system").

[6] Azevedo et al., *supra* note 3, at 29-30 (explaining that Humira "specifically binds" to tumor necrosis factor α (TNF-α) molecules).

[7] *Disease-Modifying Anti-Rheumatic Drugs (DMARDs)*, VERSUS ARTHRITIS, https://www.versusarthritis.org/about-arthritis/treatments/drugs/disease-modifying-anti-rheumatic-drugs-dmards/ [https://perma.cc/C5H7-2QWM] (last visited Jan. 30, 2022) (noting biologics "stop or block particular cells in the immune system from triggering inflammation" and "tend to work more quickly than conventional DMARDs").

[8] *Humira FDA Approval History*, DRUGS.COM, https://www.drugs.com/history/humira.html [https://perma.cc/LR5F-4T78] (last visited Jan. 30, 2022) (noting that Humira received FDA approval for treatment of: (1) rheumatoid arthritis; (2) psoriatic arthritis; (3) ankylosing spondylitis; (4) Crohn's disease; (5) moderate to severe chronic plaque psoriasis; (6) polyarticular juvenile idiopathic arthritis; (7) ulcerative colitis; (8) Crohn's disease in pediatric patients; (9) moderate to severe hidradenitis suppurativa; (10) noninfectious intermediate, posterior and panuveitis; (11) moderate to severe fingernail psoriasis; and (12) moderately to severely active ulcerative colitis in pediatric patients).

benefitted from Humira by the end of its first year of availability, and nearly one million patients benefitted by 2018.[9]

AbbVie, the manufacturer of Humira, also benefitted massively from the drug's blockbuster success and its $72,000 per year price tag,[10] generating $18.9 billion in sales in 2018 from Humira alone.[11] Humira's popularity has allowed AbbVie to increase Humira's price by 7-10% twice a year, resulting in a 79% price increase from 2011 to 2015.[12] Although regulators have criticized price increases on already expensive drugs, AbbVie is certainly not the only pharmaceutical company raising drug prices.[13] Further, as drugs reach the end of their life cycle, generic versions of the drug usually enter the market, providing direct substitutes for the brand-name agent and decreasing prices.[14] Humira has been on the market for almost twenty years now.[15] Surely, competition from generics must be looming, right?

Not so, according to a group of indirect purchasers of Humira. In June 2020, these indirect purchasers sued AbbVie in a federal district court, alleging several antitrust violations concerning AbbVie's actions to protect the U.S. market for its blockbuster autoimmune disease treatment.[16] The plaintiffs alleged that AbbVie constructed a "patent thicket"[17] around Humira by filing 247 patent

[9] Elizabeth Glasure, *BioSpace Feature: A Look at Miracle Drug Humira's Journey to Proven Efficacy*, BIOSPACE (Dec. 5, 2018), https://www.biospace.com/article/biospace-feature-a-look-at-miracle-drug-humira-s-journey-to-proven-efficacy-/ [https://perma.cc/S7RH-47KC].

[10] Christopher Rowland, *Why Price of Humira Keeps Rising Despite FDA Approval of Generic Competition*, WASH. POST (Jan. 8, 2020), https://www.washingtonpost.com /business/economy/why-humiras-price-keeps-rising-despite-fda-approval-of-generic-competition/2020/01/07/549ed0ce-2e3a-11ea-bcb3-ac6482c4a92f_story.html.

[11] Sally Turner, *Humira: The Highs and Lows of the World's Best-Selling Drug*, PHARM. TECH. (Sept. 4, 2020, 9:24 AM), https://www.pharmaceutical-technology.com/features /humira-abbvie-drug/ [https://perma.cc/JEV7-45X8] (reporting that, in 2018, Humira generated $18.9 billion, and projected sales until 2024 should generate $15.2 billion due to "continued dominance in the global marketplace").

[12] *Id.* (reporting that AbbVie has increased Humira's price in January and June of each year).

[13] *See generally* Sydney Lupkin, *A Decade Marked by Outrage over Drug Prices*, NPR (Dec. 31, 2019, 1:16 PM), https://www.npr.org/sections/health-shots/2019/12/31/792617538 /a-decade-marked-by-outrage-over-drug-prices [https://perma.cc/ZQ6B-6HDP] (describing rising drug costs in United States in 2010s).

[14] *Generic Competition and Drug Prices*, FDA, https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/generic-competition-and-drug-prices [https://perma.cc/TG2Z-WDF9] (last updated Dec. 13, 2019).

[15] *Humira FDA Approval History*, *supra* note 8.

[16] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 825-26 (N.D. Ill. 2020).

[17] Used in this Note, patent thickets refer to a multitude of overlapping patents for the same drug held by a single company, often for a strategic business advantage. *See generally* Carl

applications related to the same compound, of which 132 were granted.[18] By forming an extensive collection of overlapping patents for a single drug, the plaintiffs argued that AbbVie unfairly prevented competition even after the original Humira patents expired.[19] Unconvinced, the district court struck down each of the antitrust theories and dismissed the case.[20]

The *Humira* litigation demonstrates an increasingly worrisome trend in the pharmaceutical industry: the creation and use of patent thickets with overlapping claims to obscure patent scope, stymie competition, and maintain market exclusivity. While this practice has drawn scrutiny in years past,[21] the advent of large-molecule biologic compounds like Humira has aggravated the problem. Traditional small-molecule compounds, like Aspirin or Tylenol, have relatively simple, defined chemical structures that are disclosed in the patents for the compounds.[22] Biologics are another story entirely. These large-molecule drugs are orders of magnitude larger than their small-molecule brethren, containing numerous side chains, folds, and complexities that cannot be expressed in a single chemical formula or patent like simpler small-molecule compounds.[23] Given this complexity, biologics are massively expensive to research and produce, on the order of hundreds of millions of dollars.[24] They have been priced accordingly. For example, a one-year course of Humira costs upwards of $72,000.[25] Because the precise chemical structure of the biologic often cannot be reproduced exactly due to the biologic's complexity, producing a generic version of a biologic, called a biosimilar, is a similarly massive time- and capital-

Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, *in* 1 INNOVATION POLICY AND THE ECONOMY 119 (Adam B. Jaffe, Josh Lerner & Scott Stern eds., 2001) (defining patent thickets and describing economic theory behind patent thickets).

[18] *In re Humira*, 465 F. Supp. 3d at 822 ("One estimate suggests that AbbVie filed a total of 247 patent applications related to Humira and obtained 132 patents (a batting average of .534).").

[19] *Id.* at 819.

[20] *Id.* (holding that plaintiffs did not successfully allege antitrust violation on grounds that "[m]uch of AbbVie's petitioning was protected by the *Noerr-Pennington* doctrine, and plaintiffs' theory of antitrust injury [was] too speculative").

[21] *See, e.g.*, Shapiro, *supra* note 17, at 120-21 (criticizing use of patent thickets as means of stifling innovation with regard to e-commerce, business methods, and semiconductor industry).

[22] *What Are "Biologics" Questions and Answers*, *supra* note 4.

[23] *See* Jeffrey Wu & Claire Wan-Chiung Cheng, *Into the Woods: A Biologic Patent Thicket Analysis*, 19 CHI.-KENT J. INTELL. PROP. 93, 99-100 (2019).

[24] For example, research and development costs for eculizumab, a biologic therapy, cost approximately $817.6 million. Vinay Prasad & Sham Mailankody, *Research and Development Spending to Bring a Single Cancer Drug to Market and Revenues After Approval*, 177 JAMA INTERNAL MED. 1569, 1571 tbl. (2017).

[25] Rowland, *supra* note 10.

intensive process, requiring sophisticated equipment and facilities.[26] Functionally, this limits the already small number of companies capable of potentially competing with the original biologic manufacturer following patent expiration.[27]

Armed with patent thickets, biologic manufacturers are able to further restrain the already limited competitive landscape for their drugs. Prospective competitors may be intimidated by the formidable wall of patents; therefore, invalidation of any single patent does little to end the patent holder's power.[28] Confronted with these patents, firms face a choice: wait until the patents expire or enter the market early and risk patent infringement suits.[29] Litigating a single pharmaceutical patent costs millions of dollars,[30] with potentially more at risk if the company loses the suit and must pay damages.[31] As the number of patents increases, so too must the total cost of litigation and the potential risk of damage payments. A firm may decide that it will be easier and cheaper to forgo a few years of revenue and allow some patents to expire rather than attempt to market its drug before all the claimed patents expire and face the prospect of patent infringement suits.[32] This business decision may have more to do with the sheer volume of patents and the expense of litigation than the validity or merit of the underlying patent claims.

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[26] *See* Erwin A. Blackstone & Joseph P. Fuhr, Jr., *The Economics of Biosimilars*, 6 AM. HEALTH & DRUG BENEFITS 469, 471 (2013) ("It takes 7 to 8 years to develop a biosimilar, at a cost of between $100 million and $250 million.").

[27] *See id.* at 471-72 (listing "Complexity of Expertise" as one major barrier to market entry).

[28] AbbVie made this exact argument in the Humira antitrust litigation, arguing that if even a single Humira patent was valid, biosimilars could not have entered the market. *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 826 (N.D. Ill. 2020).

[29] Early entrance into the market is known as an at-risk launch. Keith M. Drake, Robert He, Thomas McGuire & Alice K. Ndikumana, *No Free Launch: At-Risk Entry by Generic Drug Firms* 3 (Nat'l Bureau of Econ. Rsch., Working Paper No. 29131, 2021); *see* Jeremiah Helm, Comment, *The Patent End Game: Evaluating Generic Entry into a Blockbuster Pharmaceutical Market in the Absence of FDA Incentives*, 14 MICH. TELECOMMS. & TECH. L. REV. 175, 179 (2007) (describing choice between early entry and waiting for patent expiration in generic context).

[30] *See* Malathi Nayak, *Costs Soar for Trade Secrets, Pharma Patent Suits, Survey Finds*, BLOOMBERG L. (Sept. 10, 2019, 8:01 AM), https://news.bloomberglaw.com/ip-law/costs-soar-for-trade-secrets-pharma-patent-suits-survey-finds (cases with only $1 to $10 million at risk cost median of $2.5 million).

[31] *See, e.g.*, Paul Ainsworth & Michael Bruns, *Fed. Circ. Amgen Biosimilar Ruling Raises IP Damages Risk*, LAW360 (Feb. 26, 2020, 4:53 PM), https://www.law360.com/articles/1247465/fed-circ-amgen-biosimilar-ruling-raises-ip-damages-risk (detailing $70 million damage award stemming from biosimilar patent infringement case without single infringing sale).

[32] *See, e.g.*, Helm, *supra* note 29, at 184 ("[T]hough [the generic manufacturer] received FDA approval for a generic version of Augmentin in September 2002, it delayed launch of the drug until January 2003 because it feared potential infringement liability.").

In addition to deterring competition with the sheer size of the patent thicket and the specter of patent infringement lawsuits, patent owners can also use these thickets to extend the life of a patented compound beyond the congressionally granted period of patent exclusivity[33] by claiming manufacturing processes, new formulations of the drug, or slight tweaks to the drug's delivery or structure in new patents with later filing dates.[34] Because these new patents on the same invention have later filing dates, they generate a new period of patent exclusivity; cumulatively, these additional patents extend the total exclusivity period for a drug beyond that granted by the original patent.[35] This Note refers to the process of extending a drug's exclusivity period through patenting as "evergreening."[36]

Biosimilar market entry in the United States is essential for driving down drug prices.[37] Given the intrinsic difficulty in bringing a biosimilar to market, legal structures must ensure that biologic patent owners cannot artificially prevent biosimilar competition after the companies have received a full exclusivity period to monopolize their technology. At the same time, the system must allow these manufacturers to profit off their drugs and incentivize development of these revolutionary technologies. In addition, the complexity of biologics demands some allowance for multiple patents, as their manufacturing methods and complex structure may necessitate broader coverage than small-molecule agents.[38] Accordingly, the solution must accommodate the patent rights of the patent holder without allowing the patent holder to unfairly extract more market control time than it rightfully earned and artificially limit an already narrow competitive landscape.

While some commentators have addressed the problem of patent thickets in the pharmaceutical industry, solutions typically focus on changes to the patent system.[39] Changes to patent law may be warranted, but this Note focuses on the

[33] 35 U.S.C. § 154(a)(2) (granting patent term of twenty years).

[34] *See* Wu & Cheng, *supra* note 23, at 110.

[35] *See* Uri Y. Hacohen, *Evergreening at Risk*, 33 HARV. J.L. & TECH. 479, 486-87 (2020).

[36] *See id.* at 486. As discussed in this Note, evergreening does not include additional grants of exclusivity beyond ordinary patent terms baked into the statutes regulating biosimilars or generics. *See, e.g.*, 42 U.S.C. § 262(k)(7)(A) (granting twelve-year data exclusivity period after approval of biologic). Evergreening refers solely to the affirmative act of filing additional patents with questionable therapeutic or scientific benefits over previously held patents. *See* Hacohen, *supra* note 35, at 486.

[37] *See, e.g.*, *Generic Competition and Drug Prices*, *supra* note 14 (explaining how introduction of generics into market drives prices down).

[38] *See* Wu & Cheng, *supra* note 23, at 155 ("Due to their larger size, and the existence of similar effective variants . . . the scope of a single biologic patent is relatively smaller compared to that of a small-molecule patent." (footnote omitted)).

[39] *See, e.g.*, Hacohen, *supra* note 35, at 532-38 (suggesting bounty system for invalidating patent thickets, requiring patent holder to disgorge undeserved profits); Wu & Cheng, *supra* note 23, at 174-79 (suggesting solutions such as allowing only single patent in group of related

use of antitrust laws as an ex post mechanism to prevent biologic manufacturers from gaming patent law and sticking consumers with higher prices. The possibility of antitrust enforcement would also serve as a deterrent, discouraging this misuse. Although a district court ruled that AbbVie's actions did not constitute anticompetitive behavior warranting sanction,[40] this Note argues that the formation and aggressive assertion of biologic patent thickets and the increased leverage they provide, especially the opportunity to push for delayed-entry settlement offers, constitute anticompetitive behavior. Accordingly, antitrust remedies should be available to combat each of these anticompetitive strategies given biologics' complexity, the highly regulated biosimilar approval process, and the massive savings biosimilars would offer patients who depend on these life-saving compounds.

Part I will examine the differences between generic and biosimilar regulatory approval and patenting before introducing antitrust concepts. Using the *Humira* antitrust litigation as a starting point, Part II will examine how biologic manufacturers use patent thickets and evergreening strategies to protect their expensive blockbuster biologics and unfairly prevent biosimilar competition. Finally, Part III will explain how current antitrust law can prevent patent thicket misuse.

I. SMALL MOLECULES, BIOLOGICS, PATENTS, AND ANTITRUST

While patent thickets are theoretically possible in both small-molecule and biologic contexts,[41] the complex science involved in creating biologics and biosimilars, the increased expense of bringing these drugs to market, and the differing FDA regulatory requirements combine to increase the anticompetitive harm of biologic patent thickets. Section I.A will provide an overview of how manufacturers set drug prices and high drug prices' effect on patient welfare. Section I.B will provide a brief explanation of the science underlying small-molecule drugs and the regulatory process for bringing generic drugs to market. Section I.C will examine the complex science necessary to create a biologic or a biosimilar, and Section I.D will emphasize the additional regulatory requirements necessary to bring a biosimilar to market compared to a generic drug under the Biologics Price Competition and Innovation Act ("BPCIA").[42] Section I.E will emphasize features of patent law that protect investment and encourage innovation but also allow potential abuses that result in patent thickets. Finally, Section I.F will provide a brief overview of the antitrust rules

patents to be asserted and ending exclusivity after set time period following biologic approval).

[40] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 819 (N.D. Ill. 2020).

[41] *See, e.g.*, Wu & Cheng, *supra* note 23, at 141 tbl.7 (identifying patent thickets on small-molecule and biologic drugs).

[42] Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), Pub. L. No. 111-148, 124 Stat. 804 (codified as amended at 42 U.S.C. § 262).

and policy that support the prevention of anticompetitive biosimilar suppression via patent thickets.

A. *Drug Prices*

Pricing pharmaceutical drugs can be extremely complicated, and a thorough discussion is outside the scope of this Note. However, this Section aims to provide a brief overview. Once the manufacturer develops a drug ready for market, pricing is almost entirely up to the manufacturer; typically, firms will select a price based on what the market will bear.[43] If the drug is in a crowded market, the price will be similar to other substitutes,[44] while a drug that has significant advantages over similar treatments, or a drug that is the first to treat a particular disease, can be substantially more expensive.[45] Once the manufacturer sets the list price, pharmacy benefit managers ("PBMs") negotiate discounts between the manufacturers and the insurance companies who ultimately foot the bill for many medications.[46] After negotiations, the manufacturer offers a rebate to the insurer, effectively lowering the drug's cost to the insurer.[47] For government-sponsored plans like Medicare and Medicaid, the government pays a price based on the average sales price across insurance plans, including rebates and discounts.[48]

These interactions all take place before the patient ever has to pay for the drug. But when it comes time to pay for the medication, a patient with health insurance doesn't pay the full price either: the amount the patient will pay out-of-pocket depends on the terms of their health insurance plan, including copay and deductibles, as well as whether they qualify for any additional discounts the manufacturer may offer directly to patients.[49] Accordingly, patients with health insurance rarely pay the full price for drugs covered under their plan.[50]

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[43] *See* Laura Entis, *Why Does Medicine Cost So Much? Here's How Drug Prices Are Set*, TIME (Apr. 9, 2019, 10:00 AM), https://time.com/5564547/drug-prices-medicine/ ("There are essentially no regulations governing how drugs are priced. Instead, pharmaceutical companies select a price based on a drug's estimated value, which typically translates into what they 'believe the market will bear. . . .'").

[44] *Id.* ("For drugs entering a crowded disease category with multiple other options, the calculus is different. In such cases, a new treatment will typically be priced similarly to its competitors.").

[45] *Id.* (explaining how first-in-class treatment could be priced as high as $1,000 per pill).

[46] *Id.*

[47] *Id.*

[48] *Id.*

[49] *Id.* (noting that, among other factors, "[t]he amount you pay for a brand-name drug will depend on your insurance plan; the plan's formulary, or list of drugs it prefers and covers; the size of your deductible; and the deal your insurance company has worked out with the drug's manufacturer").

[50] *See id.* ("The consumer with health insurance pays an amount that ranges from a fixed co-pay to some percentage of the full list price, depending on the terms of the plan and whether deductibles have been met.").

But this multistep process does not fully insulate patients from drug prices. First, not all health insurance plans cover all drugs equally: part of the PBM's negotiation includes placement of drugs within tiers of coverage, with higher tiers receiving greater discounts.[51] While the effectiveness of the drug is a factor, it is not the only factor;[52] a drug that might be just as effective, if not more effective than another treatment, may cost more based on the results of these negotiations. In addition, PBMs may institute a formulary exclusion, removing a particular medication from the allowed treatments for a particular disease.[53] Insurance will not cover these drugs, leaving patients to pay the full price out of pocket if they want or need that particular drug.[54] Finally, even though insurers may foot a large part of the bill, high-priced drugs can still have significant out-of-pocket costs even for patients with health insurance.[55] Accordingly, patients are still sensitive to high-priced drugs, and some may be unable to afford care that could help them treat debilitating diseases.[56]

B. *Small-Molecule Drugs*

From Aspirin to Zyrtec, many of the drugs with which consumers are most familiar contain small-molecule active ingredients.[57] Although someone

[51] *Id.*

[52] *Id.* ("Ideally, drugs would be tiered only according to their effectiveness, and there is certainly an element of that in the mix, especially for patients with Medicare. But a lot of it has to do with which manufacturers are willing to offer the greatest discounts.").

[53] *Id.*

[54] *Id.*

[55] *See* Ashley Kirzinger, Lunna Lopes, Bryan Wu & Mollyann Brodie, *KFF Health Tracking Poll – February 2019: Prescription Drugs*, KAISER FAM. FOUND. (Mar. 1, 2019), https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/ [https://perma.cc/8HDZ-BECC] (reporting that 24% of patients described financial difficulty paying for out-of-pocket prescription medication, with 10% describing it as "very difficult"). High drug costs have a detrimental effect on public health. *See* Andis Robeznieks, *AMA to Congress: Patients Pay Painful Price for High Drug Costs*, AMA (May 9, 2019), https://www.ama-assn.org/delivering-care/public-health/ama-congress-patients-pay-painful-price-high-drug-costs [https://perma.cc/ZWB9-LSK4] ("Prescription-drug price increases can lead some patients to not be able to afford critical medicine, causing them to skip doses of their medications or split pills, or force them to abandon treatment altogether.").

[56] *See* Robeznieks, *supra* note 55 ("I currently have a patient unable to afford the Enbrel or Humira that would alleviate his psoriasis and painful psoriatic arthritis—the average wholesale prices for a year of these drugs, both out for more than 15 years—has quadrupled to around $80,000 per year, and his PPO copay is 40% until he reaches his deductible . . . . So, he stopped his treatment." (quoting *Lowering Prescription Drug Prices: Deconstructing the Drug Supply Chain: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Com.*, 116th Cong. 211-12 (2019) (statement of Jack Resneck, Chair, Am. Med. Ass'n Bd. of Trs.))).

[57] *See* Huy X. Ngo & Sylvie Garneau-Tsodikova, *What Are the Drugs of the Future?*, 9 MED. CHEMISTRY COMMC'NS 757, 757 (2018) ("Small-molecule drugs include the aspirin,

unfamiliar with chemistry may find it hard to believe that compounds with names like 2-acetyloxybenzoic acid[58] could be "simple," small-molecule compounds have well-defined chemical structures that are produced through similarly well-defined chemical reactions.[59] Because of their relative simplicity, these specific chemicals are easy to claim in patents; unlike patents in other industries, pharmaceutical patents can claim the precise chemical structure, providing clear notice to other firms that this drug exclusively belongs to the patent holder.[60]

After patenting their compound, companies must gain regulatory approval from the FDA before they may market their drug in the United States.[61] In addition to the exclusivity period derived from the drug's patent,[62] FDA approval grants manufacturers an additional five-year exclusivity period of competition-free sales.[63] Concerned that pharmaceutical companies might be unable to complete the approval process (which requires extensive clinical testing) before their patents expired, the FDA-granted five-year exclusivity period provides an additional assurance that firms will be able to recover their research and development costs—even if the patents have expired, the manufacturers will be the only firm marketing their drug.[64] Once the five-year period expires, other firms can try to eat away at this government-sanctioned monopoly by producing generic versions of the drug. However, this five-year exclusivity period is separate from the patent exclusivity period; the patent term

diphenhydramine, and other molecules that we typically have in our medicine cabinets. Small-molecule drugs, including natural products, have been the pillars of traditional medicine . . . .").

[58] Or, as most know it, Aspirin. *Aspirin*, PUBCHEM, https://pubchem.ncbi.nlm.nih.gov/compound/Aspirin [https://perma.cc/MJ42-879Q] (last visited Jan. 30, 2022).

[59] *See* Michael A. Carrier & Carl J. Minniti III, *Biologics: The New Antitrust Frontier*, 2018 U. ILL. L. REV. 1, 6 (noting that "[s]mall molecules are created through a series of chemical reactions known as chemical synthesis" which is "relatively predictable, allowing generics to imitate brand drugs at low cost").

[60] JAMES BESSEN & MICHAEL J. MEURER, PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATORS AT RISK 18 (2008) ("Economists have long recognized that patents on chemicals work particularly well because these patents have very well-defined boundaries.").

[61] 21 U.S.C. § 355(a).

[62] 35 U.S.C. § 154(a)(2) (granting patent term of twenty years).

[63] 21 U.S.C. § 355(c)(3)(E)(ii) (granting five-year exclusivity period before generic application may be submitted for approval). Other exclusivities are also available from the FDA, such as a seven-year exclusivity for "orphan drugs," which are used to treat rare diseases. *See* NAT'L ORG. FOR RARE DISORDERS, ORPHAN DRUGS IN THE UNITED STATES: AN EXAMINATION OF PATENTS AND ORPHAN DRUG EXCLUSIVITY 3 (2021) (describing how seven-year exclusivity period incentivizes companies to develop rare disease treatments that would otherwise not be as profitable).

[64] *See* Carrier & Minniti, *supra* note 59, at 12-13 (describing inclusion of exclusivity period as part of push to encourage pharmaceutical innovation).

may expire before or after the FDA exclusivity period expires.[65] If patents on the drug are still in force, the generic manufacturer can still attempt to enter the market, but they face the risk of a patent infringement suit from the original biologic manufacturer.[66]

Generic drugs are "created to be the same as an already marketed brand-name drug in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use."[67] A generic drug uses the same active ingredient as the brand-name drug; however, minor differences, such as different inactive ingredients, are permitted.[68] The relative simplicity of these small-molecule active ingredients means that copying the drugs is a straightforward process: with only the name or structure in hand, chemists can produce identical compounds with identical drug activity and thus identical efficacy.[69] Once a drug's statutory exclusivity period expires, companies can petition the FDA to market these generic versions of the drug.[70] This regulatory framework is established by the Hatch-Waxman Act.[71]

Approval begins with the company seeking generic approval filing an Abbreviated New Drug Application ("ANDA").[72] Because the generic compound is chemically identical to the reference listed drug, the generic manufacturer can rely on the clinical data produced by the original drug manufacturer; generics manufacturers need only show bioequivalence of the generic to the reference listed compound, a process that does not entail any human clinical testing.[73] This reliance on older data removes the need to conduct expensive clinical trials, resulting in significant savings—potentially hundreds of millions of dollars[74]—and reducing barriers to market entry. Once approved,

[65] *Frequently Asked Questions on Patents and Exclusivity*, FDA, https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity [https://perma.cc/AD69-8BFD] (last updated Feb. 5, 2020).

[66] *See supra* note 29 and accompanying text (describing at-risk entry by generics).

[67] *Generic Drugs: Questions & Answers*, FDA, https://www.fda.gov/drugs/questions-answers/generic-drugs-questions-answers [https://perma.cc/XD5R-DF5S] (last updated Mar. 16, 2021).

[68] *Id.* (detailing how FDA ensures that generic medicines work as well as brand-name medicines).

[69] *See* PHARMACY PRAC. NEWS & SPECIALTY PHARMACY CONTINUUM, SPECIAL REPORT: UNDERSTANDING KEY DIFFERENCES BETWEEN BIOSIMILARS AND SMALL MOLECULE GENERICS 1-3 (2013) (describing why copying small-molecule drugs is easier than biologics).

[70] *See* 21 U.S.C. § 355(j) (defining Abbreviated New Drug Application ("ANDA") process for generic drug approval).

[71] *Id.*

[72] *Id.*

[73] *See* Atanu Saha, Henry Grabowski, Howard Birnbaum, Paul Greenberg & Oded Bizan, *Generic Competition in the US Pharmaceutical Industry*, 13 INT'L J. ECON. BUS. 15, 16 (2006) ("With an ANDA, generic firms need only show that their products are bioequivalent to the branded product in order to gain [FDA] approval.").

[74] *See* Helm, *supra* note 29, at 177 (estimating ANDA cost at $600,000 and new drug development cost at $800 million).

generic drug competition breaks the original manufacturer's monopoly hold of the market, driving down prices by giving patients alternatives to the brand-name agents.[75]

C. *Biologics: The Science*

In contrast to their small-molecule brethren, biologics are a diverse group of complex molecules that include "vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins."[76] These large compounds, frequently proteins, often derive their unique therapeutic properties from their complicated structures, which "can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances."[77]

Manufacturing biologics requires complicated processes involving living systems, and the precise method of manufacturing the agent often dictates components of its structure.[78] Due to this complexity, biologics cannot be characterized in simple chemical formulas or even be given traditional chemical names.[79] Accordingly, producing one of these compounds is a challenging endeavor, requiring years of research and massive amounts of capital.[80] Similarly, producing a generic version of the biologic, called a biosimilar, is much more difficult and expensive than reproducing a small-molecule drug.[81] Working from the known chemical structure and formula of a small-molecule drug, a chemist can often synthesize an exact copy of the compound with relative

[75] Although by no means a perfect system, generic small-molecule drugs have been fairly successful at reducing drug prices. *See* Saha et al., *supra* note 73, at 28 ("A month after the first generic entry, the average price of generics . . . is 76% of the brand price; by the end of the first year it is 54%; by the end of the second year it is 41%.").

[76] *What Are "Biologics" Questions and Answers*, *supra* note 4.

[77] *Id.*

[78] FDA, BIOLOGICAL PRODUCT DEFINITIONS 1, https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf [https://perma.cc/869Y-XLSP] (last visited Jan. 30, 2022).

[79] *Frequently Asked Questions About Therapeutic Biological Products*, FDA, https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/frequently-asked-questions-about-therapeutic-biological-products [https://perma.cc/2AAM-LG5E] (last updated July 7, 2015).

[80] *See, e.g.*, Prasad & Mailankody, *supra* note 24, at 1571 tbl. (listing biologic eculizumab time to approval as 15.2 years and research and development cost as $817.6 million).

[81] *See Let's See How Biosimilars Are Developed*, PFIZER, https://www.pfizerbiosimilars.com/biosimilars-development [https://perma.cc/S4WV-N24D] (last visited Jan. 30, 2022) (comparing generic development cost of $1-2 million and time of two years with biosimilar development cost of more than $100 million and time of five to nine years).

ease.[82] In contrast, even small changes to the manufacturing process for a biologic "could result in changes to the biological molecule that might not be detected by standard chemical and molecular biology characterization techniques yet could profoundly alter the safety or efficacy profile."[83] Because of this complexity, biologics are subject to a different regulatory regime than small-molecule drugs and their generic counterparts.[84]

D. *Biologics: BPCIA Regulation*

Demonstrating bioequivalence, the similarity required for generic drug approval,[85] would be nearly impossible for biologics, as tiny changes to structure with no clinical impact would technically not be bioequivalent.[86] In other words, the molecule would have to be chemically identical to demonstrate bioequivalence, a near impossibility for such complicated agents.[87] Recognizing that these differences in the science and manufacturing processes would make Hatch-Waxman regulation unfeasible for biologics, Congress passed the BPCIA to regulate and encourage competition for this new class of drugs.[88] Importantly, the BPCIA established a pathway to regulatory approval for biosimilar agents.[89] Because the precise chemical structure of the biologic often cannot be

[82] *See How Do Drugs and Biologics Differ?*, BIOTECHNOLOGY INNOVATION ORG., https://archive.bio.org/articles/how-do-drugs-and-biologics-differ [https://perma.cc/U4ZN-JGAB] (last visited Jan. 30, 2022) ("A drug is typically manufactured through chemical synthesis, which means that it is made by combining specific chemical ingredients in an ordered process. . . . Drugs generally have well-defined chemical structures, and a finished drug can usually be analyzed to determine all its various components.").

[83] *Frequently Asked Questions About Therapeutic Biological Products*, *supra* note 79.

[84] *See infra* Section I.D (describing biologic approval process under BPCIA).

[85] 21 U.S.C. § 355(j)(2)(A)(iv) (requiring that application contains "information to show that the new drug is bioequivalent to the listed drug").

[86] *See* Margo A. Bagley, *Patent Term Restoration and Non-patent Exclusivity in the US*, *in* PHARMACEUTICAL INNOVATION, COMPETITION AND PATENT LAW 111, 134 (Josef Drexl & Nari Lee eds., 2013) (describing how bioequivalence is "often not possible" because "variability inherent in biological manufacturing processes" causes small differences in structure that can significantly alter function).

[87] *See* Walter Jeske, Jeanine M. Walenga, Debra Hoppensteadt & Jawed Fareed, *Update on the Safety and Bioequivalence of Biosimilars — Focus on Enoxaparin*, 5 DRUG HEALTHCARE & PATIENT SAFETY 133, 135 (2013) ("The ultimate characteristics of biologic drugs are influenced by: choice of source material (cell line), production process, purification process, and the final pharmaceutical formulation. Differences in protein folding, aggregation, and glycosylation might manifest clinically as decreased potency/efficacy, altered pharmacokinetic behavior, or increased immunogenicity. . . . Since manufacturing processes are complex and never fully disclosed, biopharmaceuticals are considered impossible to exactly replicate . . . ." (footnotes omitted)).

[88] Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), Pub. L. No. 111-148, 124 Stat. 804 (codified as amended at 42 U.S.C. § 262).

[89] 42 U.S.C. § 262(k)(1) ("Any person may submit an application for licensure of a biological product under this subsection.").

reproduced exactly due to the agent's complexity, this regulatory framework imposes more testing and research requirements than the simpler Hatch-Waxman Act framework for small-molecule compounds.[90]

Accordingly, biosimilars must demonstrate biosimilarity, requiring that "the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product."[91] Meeting this standard requires extensive structural testing and clinical studies in humans,[92] dramatically increasing the cost of developing a biosimilar compared to a traditional generic drug.[93] However, these tests are still substantially cheaper than the cost of developing the original biologic.[94]

Drawing off experience from the Hatch-Waxman system, the BPCIA establishes a framework for resolving inevitable patent disputes, commonly referred to as the "patent dance."[95] Unlike with small-molecule drugs,[96] biologic manufacturers do not need to publish the patents covering their biologic; hopeful biosimilar manufacturers may have some idea which patents the original manufacturer will assert, but they cannot be certain until the dance begins.[97] Once a biosimilar manufacturer has developed and tested its biosimilar, it files an Abbreviated Biologic License Application with the FDA, seeking regulatory approval to launch its drug.[98] After the FDA accepts the application, the hopeful

[90] *See* Steven Kozlowski, Janet Woodcock, Karen Midthun & Rachel Behrman Sherman, *Developing the Nation's Biosimilars Program*, 365 NEW ENG. J. MED. 385, 386-87 (2011) (discussing additional testing required to establish interchangeability under BPCIA).

[91] 42 U.S.C. § 262(i)(2)(A)-(B).

[92] *Biosimilar and Interchangeable Products*, FDA, https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products [https://perma.cc/3T68-UNKX] (last updated Oct. 23, 2017) (describing usual testing required for biosimilar approval, including "human pharmacokinetic (exposure) and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies").

[93] *See* Blackstone & Fuhr, *supra* note 26, at 470-71 (discussing how $100 million to $250 million cost of developing a biosimilar "is considerably higher than the $1 million to $4 million that is required [to develop a generic drug]").

[94] *See* Prasad & Mailankody, *supra* note 24, at 1571 tbl. (listing, for example, eculizumab, a biologic which cost $817.6 million to develop).

[95] *See* Carl J. Minniti III, Sandoz v. Amgen*: Why Current Interpretation of the Biologic Price Competition and Innovation Act of 2009 Is Flawed and Jeopardizes Future Competition*, 97 J. PAT. & TRADEMARK OFF. SOC'Y 172, 178 n.48 (2015) ("The term 'Patent Dance' has been used in recent years to describe the waltz-like communication between the [original manufacturer] and biosimilar maker.").

[96] 21 U.S.C. § 355(b)(1), (c)(2) (providing that, under Hatch-Waxman system, patent information must be included in drug applications).

[97] *See* Minniti, *supra* note 95, at 178-79 (stating that one of patent dance's primary purposes is to reduce uncertainty by identifying patents that may be subject of future litigation).

[98] 42 U.S.C. § 262(k)(2)(A).

biosimilar manufacturer notifies the original biologic manufacturer and provides information about the agent.[99]

The original manufacturer, called the reference product sponsor ("RPS") in this process, must then provide a list of all the patents it reasonably believes the biosimilar producer would infringe by launching the biosimilar.[100] The applicant responds by explaining why any of the asserted patents would not be infringed or are invalid or unenforceable.[101] The RPS responds again, explaining why it believes the patents are valid, enforceable, or why the biosimilar would infringe the patent.[102] The parties negotiate in good faith to determine which patents to litigate, and litigation ensues.[103] In addition, the applicant must notify the RPS before it markets the biosimilar.[104] At this point, the RPS "may seek a preliminary injunction prohibiting the . . . applicant from engaging in the commercial manufacture or sale of [the biosimilar] until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent" on the RPS's list.[105]

E. *The Patent System*

While a full discussion of the patent system is far outside the scope of this Note, a brief overview and several provisions warrant introduction before proceeding to the discussion and mechanics of patent thickets. To obtain a patent, an inventor or their assignee files a patent application with the United States Patent and Trademark Office ("USPTO").[106] The USPTO examines the patent and assesses the patent's compliance with the patent law provisions.[107] Substantively, the main pillars of patentability are the patentable subject matter, novelty, utility, enablement, and nonobviousness requirements.[108]

Of particular relevance to this Note is the nonobviousness requirement. To satisfy the nonobviousness requirement, the claimed invention must not be obvious to a person having ordinary skill in the art in light of the prior art.[109] Functionally, this means that patents should only be granted to inventions that

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[99] *Id.* § 262(*l*)(2).

[100] *Id.* § 262(*l*)(3)(A).

[101] *Id.* § 262(*l*)(3)(B).

[102] *Id.* § 262(*l*)(3)(C).

[103] *Id.* § 262(*l*)(4).

[104] *Id.* § 262(*l*)(8)(A) ("[A]pplicant shall provide notice to the [RPS] not later than 180 days before the date of the first commercial marketing of the biological product . . . .").

[105] *Id.* § 262(*l*)(8)(B).

[106] *See Patent Process Overview*, USPTO, https://www.uspto.gov/patents/basics/patent-process-overview [https://perma.cc/JM8L-ECQP] (last visited Jan. 30, 2022).

[107] *Id.*

[108] *See* Gene Quinn, *Patentability Overview: When Can an Invention Be Patented?*, IP WATCHDOG (June 3, 2017), https://www.ipwatchdog.com/2017/06/03/patentability-invention-patented/id=84071/ [https://perma.cc/U3YV-AMVC].

[109] Leahy-Smith America Invents Act, 35 U.S.C. § 103.

provide a technological advancement to the public domain; only such a step forward is worthy of a government-sanctioned monopoly.[110] Inventions with only a predictable tweak to a previous invention should not receive patents.[111] However, assessing nonobviousness can be an extremely challenging factual inquiry, and time constraints or lack of familiarity with the subject matter may limit the USPTO's ability to adequately assess the claim before deciding whether to issue a patent.[112]

While a patent application awaits examiner approval, patent applicants sometimes file continuation applications. Continuation applications allow patent holders to add new claims to a pending patent application if the material is supported in the disclosure.[113] Continuation applications, if granted, are tied to the original patent's application date; thus, the patent term of a continuation application will be the same as the parent application.[114] Further, when an inventor seeks multiple patents with claims that may be obvious in light of the original disclosure, the inventor can add a "terminal disclaimer" to the second patent, forfeiting any exclusivity beyond the expiration of the original claims.[115] Continuation-in-part applications allow the addition of new subject matter to the disclosure and new claims based on the new subject matter; if granted, claims tied to this new subject matter receive a period of exclusivity beginning on the date of the continuation-in-part application.[116]

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[110] *See, e.g.*, Graham v. John Deere Co., 383 U.S. 1, 14 (1966) ("An invention which has been made, and which is new in the sense that the same thing has not been made before, may still not be patentable if the difference between the new thing and what was known before is not considered sufficiently great to warrant a patent." (citing S. REP. NO. 82-1979, at 6 (1952))).

[111] *See, e.g.*, KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 416 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

[112] *See* Saurabh Vishnubhakat & Arti K. Rai, *When Biopharma Meets Software: Bioinformatics at the Patent Office*, 29 HARV. J.L. & TECH. 205, 211 (2015) (noting how patent examiners have very limited time to examine patents and this may cause lax standards for approval); *see also* Mark A. Lemley & Bhaven Sampat, *Examiner Characteristics and Patent Office Outcomes*, 94 REV. ECON. & STAT. 817, 818 (2012) ("The large number of applications facing the PTO means that examiners are subject to sharp time constraints . . . the examiner spends an average of only eighteen hours over [the] years [the application is pending] working on any given application." (citation omitted)).

[113] 35 U.S.C. § 120.

[114] *See* JOHN R. THOMAS, CONG. RSCH. SERV., R40917, PATENT "EVERGREENING": ISSUES IN INNOVATION AND COMPETITION 5 (2009).

[115] The terminal disclaimer is a response to the problem of "obviousness-type double patenting," which "permits the grant of two or more patents to the same inventor, but requires that the patents expire on the same day in order to prevent the extension of patent rights beyond the lawful term of the first patent." Mark A. Lemley & Kimberly A. Moore, *Ending Abuse of Patent Continuations*, 84 B.U. L. REV. 63, 81-82 (2004) (footnote omitted).

[116] U.S. DEP'T OF COM., USPTO, MANUAL OF PATENT EXAMINING PROCEDURE § 201.08 (9th ed. rev. 10-2019, 2020) [hereinafter MPEP], https://www.uspto.gov/web/offices/pac/mpep/index.html [https://perma.cc/8A5A-736Y].

Once the examiner is satisfied that the requirements are met, the patent issues.[117] Once issued, the patent holder has the "right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States"[118] for a period of twenty years from the filing date of the patent.[119] Others may challenge the validity of the patent by suing the patent holder or initiating one of several administrative proceedings; if successful, they may invalidate one or more of the patent's claims, potentially enabling them to practice the previously exclusive invention.[120]

While twenty years of exclusivity may seem like a substantial monopoly period, pharmaceutical companies face numerous time-consuming regulatory hurdles before they can bring their drug to market. These companies have powerful incentives to patent their drugs as soon as they invent them, lest they be anticipated by another inventor or their own research efforts[121] and encounter a patentability issue when they do try to patent.[122] Accordingly, companies often file patents before they even begin the regulatory process. By the time the drug gains approval, eight or more years have often passed,[123] substantially reducing the time in which the company can market the drug and recover its investment in the drug's development.

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[117] *See Patent Process Overview*, *supra* note 106.

[118] 35 U.S.C. § 154(a)(1).

[119] *Id.* § 154(a)(2).

[120] For example, a party can challenge some aspects of a patent through a process known as inter partes review ("IPR"). *See Inter Partes Disputes*, USPTO, https://www.uspto.gov/patents/laws/america-invents-act-aia/inter-partes-disputes [https://perma.cc/E6Z8-UN9E] (last visited Jan. 30, 2022). These challenges have proven extremely successful at invalidating patent claims—one analysis found that, between November 2013 and June 2019, only about 25% of claims challenged in IPR proceedings survived. Daniel F. Klodowski, David C. Seastrunk & Michael R. Galgano, *Special Report – PTAB IPR Stats over Time for Q2 2019*, FINNEGAN (Aug. 13, 2019), https://www.finnegan.com/en/insights/blogs/at-the-ptab-blog/special-report-ptab-ipr-stats-over-time-for-q2-2019.html [https://perma.cc/2ZQ7-YYYV].

[121] An invention must be patented within one year of its disclosure. 35 U.S.C. § 102(b)(1). Thus, if a company discloses the results of its research in some way, such as publishing the findings, the company's own research efforts can block it from patenting the invention. Similarly, secret commercial use of the invention can count as disclosure and prevent the inventor from later obtaining a patent. *See, e.g.*, Pennock v. Dialogue, 27 U.S. (2 Pet.) 1, 14 (1829); Metallizing Eng'g Co. v. Kenyon Bearing & Auto Parts Co., 153 F.2d 516, 520 (2d Cir. 1946).

[122] *See, e.g.*, Jacob S. Sherkow, *What the CRISPR Patent Dispute Is All About*, SCI. AM. (Dec. 12, 2016), https://blogs.scientificamerican.com/guest-blog/what-the-crispr-patent-dispute-is-all-about/ [https://perma.cc/29JE-5SA5] (describing extensive patent litigation surrounding who invented CRISPR technology).

[123] Wu & Cheng, *supra* note 23, at 154 (finding average time from first patent to market launch for drugs examined in study was 8.17 years).

Recognizing the difficult and time-consuming regulatory process encountered by pharmaceutical patent holders, Congress has enacted several provisions to counter this loss of exclusivity. A patent holder may file for a patent term extension of up to five years to counteract the time lost while completing the regulatory process.[124] While not patent term extensions, both the Hatch-Waxman Act and the BPCIA have mandatory exclusivity periods following approval to guarantee a period of monopoly marketing, producing a similar economic effect as a patent term extension.[125]

F. *Antitrust Law*

While patent law sometimes grants a government-sanctioned monopoly to inventors, antitrust law exists to prevent companies from attempting to "gain or maintain monopoly power by inappropriately suppressing competition."[126] Patents are not supposed to inappropriately suppress competition; the state-sanctioned monopoly[127] provides incentives for inventors to disclose their technology and rewards for developing it. However, this Note suggests that the use of patent thickets to artificially extend the monopoly on biologics crosses into inappropriate suppression of competition and presents an opportunity for antitrust enforcement. Accordingly, this Section provides a brief background on antitrust law.

What's wrong with monopoly? Generally, consumer demand for a product will decrease as price increases.[128] Conversely, manufacturers will produce more of a given good as prices increase.[129] These competing forces will stabilize at the price where consumer demand matches manufacturer supply, called the equilibrium point.[130] However, when a monopolist completely controls the

[124] 35 U.S.C. § 156(g)(6).

[125] 21 U.S.C. § 355(c)(3)(E)(ii) (granting five-year exclusivity period before generic application may be approved); 42 U.S.C. § 262(k)(7)(A) (granting twelve-year exclusivity period before biosimilar application may be submitted). However, in practice, these exclusivity periods often do "not adequately compensate the loss of patent term since they usually overlap with each other." Wu & Cheng, *supra* note 23, at 155.

[126] Robin Feldman, *Patent and Antitrust: Differing Shades of Meaning*, 13 VA. J.L. & TECH. 1, 4 (2008).

[127] In many industries, a patent does not actually create a monopoly. Although the inventor may prevent anyone else from using the technology claimed in the patent, and thus exercise a monopoly over that particular technology, substitutes prevent monopolization of the broader market. For example, an inventor with a patent on a type of gloves would not suddenly control the entire market for gloves; alternatives exist. In the pharmaceutical industry, however, a patent may actually create a monopoly; a company that discovers and patents a novel disease treatment may be the only option for patients with that disease.

[128] Jason Fernando, *Law of Supply and Demand*, INVESTOPEDIA, https://www.investopedia.com/terms/l/law-of-supply-demand.asp [https://perma.cc/W24G-A3QX] (last visited Jan. 30, 2022).

[129] *Id.*

[130] *Id.*

market, they can set a price higher than the equilibrium price because there are no substitutes for consumers to purchase.[131] Even though some consumers are not willing to pay the higher price and the monopolist sells fewer goods, the higher profit margin still generates additional profits at the cost of consumer welfare.[132]

Accordingly, the goal of antitrust enforcement is to preserve competitive markets and allow firms to compete with the would-be monopolist on the merits of their business.[133] However, acquiring a monopoly through legitimate business success or superior products does not necessarily result in antitrust scrutiny; punishment is reserved for companies that obtain their monopoly position "by exclusionary or predatory acts."[134] By fostering competition in less competitive markets, consumers benefit as firms are forced to compete with each other in terms of price and quality.[135]

The heart of antitrust law and the central antitrust authority on which this Note focuses is the Sherman Antitrust Act of 1890 ("Sherman Act"). Under section 1 of the Sherman Act, "[e]very contract, combination in the form of trust or otherwise, or conspiracy, in restraint of trade or commerce among the several States, or with foreign nations, is declared to be illegal."[136] Some agreements are so anticompetitive on their face that they are considered per se antitrust violations.[137] However, these agreements are the exception; most agreements inspire a more flexible rule of reason analysis, which examines whether the

[131] *See* Neel U. Sukhatme, *Regulatory Monopoly and Differential Pricing in the Market for Patents*, 71 WASH. & LEE L. REV. 1855, 1864 (2014) ("A monopolist has market power because it is the sole seller of a particular good or service. Customers cannot purchase that good or service elsewhere, at least at comparable cost." (footnote omitted)).

[132] *See* Thomas O. Barnett, Assistant Att'y Gen., DOJ, Presentation to the George Mason University Law Review 11th Annual Symposium on Antitrust: Maximizing Welfare Through Technological Innovation (Oct. 31, 2007), https://www.justice.gov/atr/speech/maximizing-welfare-through-technological-innovation [https://perma.cc/6WBL-ZLKE] (describing how "monopolist[s] will choose to forego some additional customers in order to keep the price high" which decreases the consumer surplus, the gap between what consumers actually pay and maximum they would pay).

[133] *See* Feldman, *supra* note 126, at 18-19 ("Modern antitrust law does not condemn a firm for gaining or maintaining monopoly power through skill, luck, or hard work. Rather, antitrust law defines certain types of behavior that are forbidden on the road to domination." (footnote omitted)).

[134] *Monopolization Defined*, FTC, https://www.ftc.gov/tips-advice/competition-guidance/guide-antitrust-laws/single-firm-conduct/monopolization-defined [https://perma.cc/VU5X-YXAM] (last visited Jan. 30, 2022).

[135] *About the Division: Mission*, DOJ: ANTITRUST DIV., https://www.justice.gov/atr/mission [https://perma.cc/64L9-8C9X] (last updated July 20, 2015).

[136] Sherman Antitrust Act of 1890, 15 U.S.C. § 1.

[137] *See, e.g.*, NYNEX Corp. v. Discon, Inc., 525 U.S. 128, 133 (1998) ("[C]ertain kinds of agreements will so often prove so harmful to competition and so rarely prove justified that the antitrust laws do not require proof that an agreement of that kind is, in fact, anticompetitive in the particular circumstances.").

procompetitive justifications for a particular agreement outweigh the anticompetitive harms.[138]

Of particular importance to this Note, "[r]everse-payment settlements (where the patentee pays the alleged infringer rather than the other way around) trigger § 1 antitrust scrutiny and rule of reason analysis."[139] Reverse payment schemes were scrutinized in the small-molecule context in *FTC v. Actavis, Inc.*[140] There, a brand-name drug manufacturer paid a generic drug manufacturer to delay entry to the U.S. market.[141] The *Humira* court reasoned that "the *Actavis* settlement suggested that the patents were at risk and that the patentee purchased an opportunity to keep prices set at its preferred level—sharing monopoly profits with a competitor without consumer gains."[142] The Supreme Court in *Actavis* used the size of the payment as a proxy for assessing the weakness of the patent and reasoned that an actual determination of patent validity would not usually be necessary.[143]

Section 2 of the Sherman Act prohibits monopolization of interstate commerce.[144] To allege a section 2 claim, a plaintiff must show "(1) the possession of monopoly power in the relevant market and (2) the willful acquisition or maintenance of that power as distinguished from growth or development as a consequence of a superior product, business acumen, or historic accident."[145] Thus, the Sherman Act prohibits the use of unfair, anticompetitive tactics to gain or preserve monopoly power. In the biologics context, both the acquisition and the subsequent assertion of the patents in the patent thicket could fall within this prohibition.

Patent law and antitrust law appear at first glance to be diametrically opposed: antitrust focuses on preventing monopolization, while patents grant a limited monopoly to the patent owner in exchange for contributing the information

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[138] *See, e.g.*, State Oil Co. v. Khan, 522 U.S. 3, 10 (1997) ("[T]he finder of fact must decide whether the questioned practice imposes an unreasonable restraint on competition, taking into account a variety of factors, including specific information about the relevant business, its condition before and after the restraint was imposed, and the restraint's history, nature, and effect."); *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 839 (N.D. Ill. 2020) ("Procompetitive justifications (e.g., the avoidance of litigation costs) can be examined and accounted for as part of the rule of reason analysis.").

[139] *In re Humira*, 465 F. Supp. 3d at 838.

[140] 570 U.S. 136 (2013).

[141] *Id.* at 144-45.

[142] *In re Humira*, 465 F. Supp. 3d at 838.

[143] *Actavis*, 570 U.S. at 158 ("In sum, a reverse payment, where large and unjustified, can bring with it the risk of significant anticompetitive effects; one who makes such a payment may be unable to explain and to justify it; such a firm or individual may well possess market power derived from the patent; a court, by examining the size of the payment, may well be able to assess its likely anticompetitive effects along with its potential justifications without litigating the validity of the patent; and parties may well find ways to settle patent disputes without the use of reverse payments.").

[144] Sherman Antitrust Act of 1890, 15 U.S.C. § 2.

[145] United States v. Grinnell Corp., 384 U.S. 563, 570-71 (1966).

contained in the patent disclosure to the public.[146] Functionally, this limited monopoly grant must be immune from antitrust scrutiny in the vast majority of cases. Like other methods of petitioning the government, under the *Noerr-Pennington* doctrine, prosecuting patents is typically protected speech under the First Amendment.[147] However, it is possible to abuse this power to unfairly harm competition[148]: "[P]etitioning the government (during patent prosecutions, the FDA approval process, and in the courts) can violate the antitrust laws if, in reality, that petitioning is nothing more than a sham meant to inhibit competition."[149]

Under the Clayton Antitrust Act of 1914, private litigants may bring private actions for antitrust violations seeking damages[150] or injunctive relief.[151] In order to have standing to sue, plaintiffs must allege that they suffered an antitrust injury "of the type the antitrust laws were intended to prevent and that flows from that which makes defendants' acts unlawful."[152] Antitrust injuries require a close causal connection to the actions of the alleged monopolist: courts examine whether the alleged "violation was the cause-in-fact of the injury: that 'but for' the violation, the injury would not have occurred."[153] Requiring that plaintiffs show that they experienced harm can be demanding, and courts will dismiss claims based on "some abstract conception or speculative measure of harm."[154]

In addition to private litigation, both the Department of Justice ("DOJ") and the Federal Trade Commission ("FTC") are tasked with enforcing antitrust

[146] *See* Feldman, *supra* note 126, at 2 ("The relationship between patent law and antitrust law has challenged legal minds since the emergence of antitrust law in the late nineteenth century. In reductionist form, the two concepts pose a natural contradiction: One encourages monopoly, while the other restricts it.").

[147] *See In re Humira*, 465 F. Supp. 3d at 828.

[148] *See, e.g.*, United States v. Line Material Co., 333 U.S. 287, 308 (1948) (noting that "possession of a valid patent or patents does not give the patentee any exemption from the provisions of the Sherman Act beyond the limits of the patent monopoly"); Atari Games Corp. v. Nintendo of Am., Inc., 897 F.2d 1572, 1576 (Fed. Cir. 1990) ("When a patent owner uses his patent rights not only as a shield to protect his invention, but as a sword to eviscerate competition unfairly, that owner may be found to have abused the grant and may become liable for antitrust violations when sufficient power in the relevant market is present.").

[149] *In re Humira*, 465 F. Supp. 3d at 828.

[150] Clayton Antitrust Act of 1914, 15 U.S.C. § 15(a) ("[A]ny person who shall be injured . . . by reason of anything forbidden in the antitrust laws may sue therefor . . . .").

[151] *Id.* § 26 ("[A]ny person, firm, corporation, or association shall be entitled to sue for and have injunctive relief . . . against threatened loss or damage by a violation of the antitrust laws . . . .").

[152] Brunswick Corp. v. Pueblo Bowl-O-Mat, Inc., 429 U.S. 477, 489 (1977).

[153] Greater Rockford Energy & Tech. Corp. v. Shell Oil Co., 998 F.2d 391, 395 (7th Cir. 1993).

[154] Associated Gen. Contractors of Cal., Inc. v. Cal. State Council of Carpenters, 459 U.S. 519, 543 (1983) (quoting Blue Shield of Va. v. McCready, 457 U.S. 465, 475 n.11 (1982)).

regulations.[155] Like private litigants, the DOJ and FTC must prove an antitrust violation.[156] Unlike private litigants, however, these federal agencies need not demonstrate antitrust injury and thus are free of the strict causal analysis imposed upon private litigants.[157] The agencies have developed particular focuses on certain industries, with the FTC demonstrating a particular interest in healthcare and pharmaceutical antitrust issues.[158] The FTC can seek injunctions or consent decrees requiring the monopolist cease their anticompetitive behavior.[159] The FTC can also pursue disgorgement of profits obtained as a result of antitrust violations.[160]

Together, these enforcement mechanisms promote competition and protect consumers from the harms of monopoly pricing. In addition, promoting competition also encourages innovation as companies work to outpace rivals.[161] For biologics, the promotion of competition via biosimilar market entry is essential for balancing incentives, encouraging the development of innovative new medicines, and decreasing drug prices.

II. BIOLOGIC PATENT THICKETS PREVENT NEEDED COMPETITION

Biologics and their biosimilar relatives require complicated science to produce, and the legal and regulatory regimes governing them are necessarily complex as well. Because of difficult manufacturing processes, complex science, and a unique regulatory environment, Section II.A of this Note will demonstrate that the biologics market inherently produces very limited competition and that biosimilar competition is essential for increasing patient choice and access to these medicines. Section II.B will describe how biologic manufacturers' patent thickets can extend their patent monopolies through evergreening, artificially constraining this already narrow market. Using the

[155] PATRICIA M. DANZON, COMPETITION AND ANTITRUST ISSUES IN THE PHARMACEUTICAL INDUSTRY 24 (2014).

[156] Dan Butrymowicz, *Antitrust Violation vs. Injury-in-Fact: A Distinction That Makes a Difference*, FTC (Feb. 26, 2016, 11:16 AM), https://www.ftc.gov/news-events/blogs/competition-matters/2016/02/antitrust-violation-vs-injury-fact-distinction-makes [https://perma.cc/VWF8-SBCE].

[157] *Id.* ("But private plaintiffs must make an additional showing: to establish antitrust 'standing,' private plaintiffs must prove that the antitrust violation caused *harm to them*.").

[158] DANZON, *supra* note 155, at 24.

[159] *The Enforcers*, FTC, https://www.ftc.gov/tips-advice/competition-guidance/guide-antitrust-laws/enforcers [https://perma.cc/MEY7-DM47] (last visited Jan. 30, 2022).

[160] *A Brief Overview of the Federal Trade Commission's Investigative, Law Enforcement, and Rulemaking Authority*, FTC, https://www.ftc.gov/about-ftc/what-we-do/enforcement-authority [https://perma.cc/KZ3L-87HY] (last updated May 2021).

[161] This is true to a point; although too much competition can harm innovation, moving from monopoly to moderate competition improves innovation. *See* Herbert Hovenkamp, *Competition for Innovation*, 2012 COLUM. BUS. L. REV. 799, 802 (noting that "the rate of innovation is highest in moderately concentrated markets, and tapers off as the market tends toward either monopoly or more atomistic competition").

Humira litigation as an example, Section II.C will then explore how biologic manufacturers can wield these patent thickets to actively prevent biosimilar competition, unfairly enriching themselves at the cost of patient choice.

A. *Biologics: A Limited Competitive Market*

As explained above, biologics are incredibly complex, costing manufacturers millions of dollars and numerous years to research and produce.[162] Details of the manufacturing process dictate the structure of the biologic and thus also dictate the biologic's effectiveness.[163] As a result, only sophisticated companies with access to both resources and production expertise can produce biologics, limiting potential competition. While small biotech startups have always faced difficulties developing and subsequently marketing new small-molecule drugs,[164] these additional constraints make upstart challengers even less likely in the biologic context.

A single manufacturer's domination of the market for a particular drug would not draw antitrust scrutiny if there were effective substitutes for that drug.[165] For example, if the manufacturer of an allergy medication controlled the entire market for a particular compound, the vast array of allergy medications available to patients would provide substitutes for price-sensitive consumers and limit the ability of the would-be monopolist to raise prices on their compound.[166] However, biologics often do not have readily available substitutes.[167] Many biologics are revolutionary drugs, resulting in significantly improved outcomes

[162] *See supra* notes 24-26 and accompanying text.

[163] *See supra* Section I.C (discussing biologic manufacturing process).

[164] *See, e.g.*, MEIR STATMAN, COMPETITION IN THE PHARMACEUTICAL INDUSTRY: THE DECLINING PROFITABILITY OF DRUG INNOVATION 48 (1983) (discussing how research and development costs and lack of experience prevent small pharmaceutical companies from entering some markets).

[165] *Markets*, FTC, https://www.ftc.gov/tips-advice/competition-guidance/guide-antitrust-laws/mergers/markets [https://perma.cc/TS25-BF6D] (last visited Jan. 30, 2022) ("The loss of competition may not matter if a sufficient number of customers are likely to switch to products or services sold by other companies. . . .").

[166] *See* Entis, *supra* note 43 ("For drugs entering a crowded disease category with multiple other options, the calculus is different. In such cases, a new treatment will typically be priced similarly to its competitors.").

[167] For example, consider treatment for spinal muscular atrophy. Patients have two options: a one-time treatment with the biologic Zolgensma for $2.1 million dollars, or a lifetime of treatment with the less-effective small-molecule drug Spinraza. *See* Joshua Cohen, *At over $2 Million Zolgensma Is the World's Most Expensive Therapy, Yet Relatively Cost-Effective*, FORBES (June 5, 2019, 10:32 AM), https://www.forbes.com/sites/joshuacohen/2019/06/05/at-over-2-million-zolgensma-is-the-worlds-most-expensive-therapy-yet-relatively-cost-effective/ ("[S]pending money on Zolgensma implies the need to assess the value of the next best alternative; in this case, Spinraza. As Spinraza is not a one-off treatment it must be administered on a regular basis. It also doesn't restore functioning to the same degree as Zolgensma.").

compared to older-generation small-molecule drugs, sometimes becoming the standard of care for diseases with a previously grim prognosis.[168]

Because of this unmatched effectiveness, demand for biologics is inelastic: higher prices do not result in significantly fewer sales for life-saving or incredibly effective treatments.[169] This allows manufacturers great freedom in assigning prices to their drugs; when you have the only cure for a life-threatening condition, patients are willing to pay any asking price.[170] Even when multiple companies are able to produce biologics targeted to the same protein and operating by the same mechanism of action, the vast complexity of the agents results in surprisingly disparate outcomes and prevents them from being perfect substitutes.[171]

However, demand for the drugs is not perfectly inelastic: some patients, unable to afford these high-cost treatments or unwilling to spend thousands of dollars per dose, are forced to make do with outdated drugs with lower efficacy or entirely forgo treatment of a chronic condition.[172] Pricing patients out of the most effective treatment is a public health issue; without competition from other biologics manufacturers, biosimilars present the best opportunity for creating competitive substitutes for these vital biologic medicines. While biosimilar competition will not entirely alleviate an issue systemic to the American healthcare system, lower prices and more patient options certainly improve patient access to important medicine.[173]

Although creating a biosimilar presents the opportunity to create a competitive substitute for the biologic in question, biosimilar manufacturers are subject to many of the same constraints as biologic manufacturers. Functionally, the complexity of the original compounds limits the potential competition these biologic manufacturers might face by decreasing the number of firms capable of

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[168] *See, e.g.*, Howard (Jack) West, *Management of Advanced Non-small Cell Lung Cancer Lacking a Driver Mutation: Immunotherapy*, UPTODATE, https://www.uptodate.com/contents/management-of-advanced-non-small-cell-lung-cancer-lacking-a-driver-mutation-immunotherapy [https://perma.cc/WBG6-RSSC] (last updated Sept. 15, 2021) (describing biologic pembrolizumab's role as standard of care for treating advanced lung cancer).

[169] *See* Wu & Cheng, *supra* note 23, at 153 (describing inelasticity of demand for biologics and effects on patient health).

[170] *See, e.g.*, Cohen, *supra* note 167 (explaining that $2.1 million for single treatment of Zolgensma makes sense for some patients with spinal muscular atrophy because, "[o]ver a 10-year period Spinraza's costs would total over $4 million").

[171] For example, the FDA has approved six biologics that operate by very similar mechanisms, targeting the PD-1/PD-L1 axis. Leilei Ai, Jian Chen, Hao Yan, Qiaojun He, Peihua Luo, Zhifei Xu & Xiaochun Yang, *Research Status and Outlook of PD-1/PD-L1 Inhibitors for Cancer Therapy*, 14 DRUG DESIGN DEV. & THERAPY 3625, 3627 (2020). Despite the similarity in mechanism of action, the drugs have vastly different FDA approvals, reflecting disparate clinical results in similar patient groups. *See id.* at 3627-37 (reviewing clinical data and indications for approved PD-1/PD-L1 inhibitors).

[172] *See* Wu & Cheng, *supra* note 23, at 153 (describing inelasticity of demand for biologics and effects on patient health).

[173] *Id.*

producing a biosimilar. In addition, the biosimilar development timeline is much longer than for small-molecule compounds, reducing the speed with which a competitor can bring a biosimilar to market.[174] The development speed is further limited by the twelve-year data exclusivity period granted to a newly approved biologic.[175]

The complexity of biologics also complicates the patent process. Small-molecule drug patents provide exceptionally clear notice because small-molecule drug patents claim discrete chemical structures.[176] In contrast, biologics are extremely complex, with only certain structures contributing to safety and efficacy.[177] Accordingly, biologic patent practices tend to focus more on the manufacturing process than the actual compound because similar agents may deviate in some structural aspects that do not affect the agent's utility.[178] Thus, rather than claiming a simple chemical, biologic patents are drafted to prevent similar manufacturing processes and block similar agents;[179] this necessarily results in fuzzier boundaries and less clear patent scopes.[180]

As a result, biosimilar manufacturers must conduct much more independent research into how to create a biosimilar, and wade through more patents and claims, before they can produce a compound they are confident works and does not infringe any patents. Manufacturers must identify not only the patents covering the reference biologic in question but also any process patents that might block them from creating a biosimilar.[181] In addition, many of these critical processes are protected by trade secrets rather than being disclosed in patents, forcing biosimilar manufacturers to attempt to reverse engineer the process.[182] Later-filed process patents present a further problem: biosimilar

[174] *See* Blackstone & Fuhr, *supra* note 26, at 471 ("It takes 7 to 8 years to develop a biosimilar, at a cost of between $100 million and $250 million.").

[175] 42 U.S.C. § 262(k)(7)(A).

[176] *See* BESSEN & MEURER, *supra* note 60, at 18 ("In addition, the pattern of litigation costs across technologies is consistent with differences in patent notice. Litigation costs are particularly low for patents on chemical compounds, including pharmaceuticals.").

[177] *See supra* Section I.C.

[178] Wu & Cheng, *supra* note 23, at 160 (finding that biologics employed core manufacture patents while generic agents did not).

[179] *Id.* at 162 ("Being 'similar' allows the possibility to be different from the reference biologic product, meaning that there can be patents that do not claim the reference biologic product itself but are potential threats to the entry for biosimilars." (footnote omitted)).

[180] *Id.* at 155 ("[T]he scope of a single biologic patent is relatively smaller compared to that of a small-molecule patent.").

[181] *See id.* at 163 (discussing how biosimilar manufacturers "have to hack through or scrutinize not only the patents claiming the reference biologic product itself, but also patents that claim its variations").

[182] *See* Evelien Moorkens, Clara Jonker-Exler, Isabelle Huys, Paul Declerck, Steven Simoens & Arnold G. Vulto, *Overcoming Barriers to the Market Access of Biosimilars in the European Union: The Case of Biosimilar Monoclonal Antibodies*, 7 FRONTIERS

manufacturers cannot be certain whether these patents represent an actual novel step forward compared to the original, secret process or if the patent owner merely tried to capture the original process it had been employing.[183] These additional patent considerations further increase the difficulty and expense of producing a biosimilar.

Even after a biosimilar company has conducted a thorough patent search and believes they understand the risks of attempting to bring the biosimilar to the market, the outcome of potential patent litigation is still unpredictable. While the patent dance process provides a clear structure for the litigation, the lack of initial notice presents a challenge for hopeful biosimilar manufacturers. Generic drug companies know the exact patents that the original manufactures will assert and are able to design their manufacturing process and formulation around these patents.[184] Hopeful biosimilar manufacturers, on the other hand, must conduct their own independent searches to identify patents they believe might be asserted as they plan their biosimilar, long before the patent dance begins.[185] As discussed above, this search process could be expensive, and it is very easy to miss or misinterpret a patent that could later be asserted.[186] Once the dance begins, a surprise patent could force additional legal assessment and potentially demand tweaks to the manufacturing process, both expensive endeavors. This unclear notice combined with the expense of producing and testing the biosimilar necessarily contributes to the increased cost of bringing a biosimilar to market compared to the cost of generic drug approval.

In light of this litigation uncertainty and the prospect for prolonged battles with the biologic manufacturer, a hopeful biosimilar market entrant must choose when to seek approval and begin marketing their biosimilar. From a competitive market and patient choice standpoint, one large problem influencing this analysis is that the biosimilar manufacturer's goals are not aligned with patients' goals. Although patients ultimately benefit from the increased competition and

PHARMACOLOGY 1, 3 (2016) ("Biosimilar developing companies have no access to the original biological expression system that was used for the innovative reference product and therefore need to take a reverse engineering approach. Thus, full knowledge of the production process of the innovator medicine is not available as it is mainly protected by trade secret." (citation omitted)).

[183] Arti K. Rai & W. Nicholson Price II, *An Administrative Fix for Manufacturing Process Patent Thickets*, 39 NATURE BIOTECHNOLOGY 20, 21 (2021) ("When confronted with [a manufacturing process] patent, a competitor cannot know whether the examiner simply granted the patent erroneously, lacking knowledge that the process or a related version was already being used commercially, or whether the patent covers a significant, non-obvious postapproval modification . . . .").

[184] *See* Wu & Cheng, *supra* note 23, at 163 (describing how small-molecule generic manufacturers "only need to worry about the patents that cover the brand name . . . drug" because the generic must be equivalent rather than similar).

[185] *See id.* at 162.

[186] *See id.* at 163 (noting that biosimilar manufacturers must "scrutinize not only the patents claiming the reference biologic product itself, but also patents that claim its variations" when designing their biosimilar).

lower prices biosimilars bring, the biosimilar manufacturers seek only to maximize their profit. Ideally, biosimilars present a win for both patients and the manufacturers, but these disparate motivations mean that biosimilar producers may choose not to litigate when patients would benefit from the opposite decision and increased competition.[187]

Finally, biosimilars are not automatically interchangeable with brand-name drugs like they are in the generics context.[188] Without interchangeability, doctors must write prescriptions for the biosimilar specifically; pharmacists do not have the option to substitute the biosimilar for a prescription for the original biologic.[189] Establishing interchangeability requires even more exhaustive clinical testing, comparing the original biologic directly to the biosimilar.[190] In addition to the expense, healthcare professionals and patients may be reluctant to participate in clinical trials where the best case scenario is receiving an equivalent drug.[191] To date, only one approved biosimilar has achieved interchangeability status.[192] Thus, almost every biosimilar company must

[187] *See id.* at 166-67 (describing conflicts of interest biosimilar manufacturers face).

[188] *See* Carrier & Minniti, *supra* note 59, at 15-16 (describing approval process to establish biosimilar interchangeability and pointing out that no biosimilar has yet met this burden).

[189] *Biosimilar and Interchangeable Biologics: More Treatment Choices*, FDA, https://www.fda.gov/consumers/consumer-updates/biosimilar-and-interchangeable-biologics-more-treatment-choices [https://perma.cc/J52H-GRL4] (last updated Oct. 12, 2021) ("An interchangeable biosimilar product may be substituted without the intervention of the health care professional who prescribed the reference product . . . .").

[190] Manufacturers face the additional hurdle of showing the biologic "can be expected to produce the same clinical result as the reference product in any given patient." 42 U.S.C. § 262(k)(4)(A)(ii). If the biologic is administered in multiple doses, manufacturers must further show that "the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch." *Id.* § 262(k)(4)(B). Meeting these additional hurdles requires additional clinical studies. *See, e.g.*, Tony Hagen, *The Difference Between an Interchangeable Biosimilar and One That Isn't*, AJMC: CTR. FOR BIOSIMILARS (May 5, 2021), https://www.centerforbiosimilars.com/view/the-difference-between-an-interchangeable-biosimilar-and-one-that-isn-t [https://perma.cc/VTM9-WK6G] (describing design of "separate [clinical] study that involved patients switching multiple times from reference drug to biosimilar and back again" performed to satisfy interchangeability requirements).

[191] *See* Liese Barbier, Hans C. Ebbers, Paul Declerck, Steven Simoens, Arnold G. Vulto & Isabelle Huys, *The Efficacy, Safety, and Immunogenicity of Switching Between Reference Biopharmaceuticals and Biosimilars: A Systematic Review*, 108 CLINICAL PHARMACOLOGY & THERAPEUTICS 734, 734 (2020) (describing concerns patients and healthcare professionals have with switching from reference biologic to biosimilar).

[192] Press Release, Viatris Inc. & Biocon Biologics Ltd., Viatris Inc. and Biocon Biologics Receive Historic Approval for First Interchangeable Biosimilar Semglee® (Insulin Glargine-yfgn) Injection for the Treatment of Diabetes (July 28, 2021), https://newsroom.viatris.com/2021-07-28-Viatris-Inc-and-Biocon-Biologics-Receive-Historic-Approval-for-First-Interchangeable-Biosimilar-Semglee-R-insulin-glargine-yfgn-injection-for-the-Treatment-of-Diabetes [https://perma.cc/65SR-J8AJ] (describing FDA approval of insulin biosimilar as interchangeable).

convince both patients and doctors that a prescription for the biosimilar will be just as effective as a prescription for the biologic. This additional barrier means that even after biosimilars are approved and available on the market, patients may not immediately switch to biosimilars as quickly as they would generics. Thus, brand-name biologics will still have a substantial market for some time even after biosimilar market entry.

B. *Patent Thickets and Evergreening*

Given the myriad barriers to entry, the market for biologics is sorely constrained. Despite this limited competition, all of the barriers discussed in the previous Section are legitimate. The barriers are due to the complex science and regulatory environment—not anticompetitive actions by monopolists. Thus, a monopoly from these regulatory factors should not be subject to antitrust scrutiny. However, these narrow biologic markets are particularly susceptible to gamesmanship by biologics manufacturers heavily motivated to maintain their monopolies and continue selling drugs at monopoly prices.

Taking advantage of the same regulatory environment and scientific constraints that narrow the market, biologic manufacturers further restrict competition by generating patent thickets. As used in this Note, patent thickets refer to a multitude[193] of overlapping patents for the same drug held by a single company, often for a strategic business advantage. The term patent thicket sometimes refers to a crowded patent field where multiple parties have patents with overlapping rights.[194] While also potentially problematic, this Note is focused on the actions of single companies.

Originally discussed in the high-tech context,[195] patent thickets have become increasingly problematic in the pharmaceutical industry, particularly for biologics. In an effort to maintain effective monopoly over these medicines, manufacturers employ patent thickets to improve their bargaining position and prevent competition. Companies build these thickets by filing numerous patents

[193] While a greater number of patents for the same invention is suggestive of a patent thicket, given the complexity of biosimilar agents, this Note does not assign an exact number of patents to the definition of a patent thicket. Instead, patent thickets should be identified by examining the number of related patents and their relationship to each other. A high number of very closely related patents, bordering on obvious-like double patenting, is most suggestive of a patent thicket. Putting an actual number would be helpful for bright line rule purposes but also does not fully appreciate the nuance. *See* Wu & Cheng, *supra* note 23, at 164-65 (recognizing that "[i]t is difficult to draw a clear-cut line as to how many patents amount to a patent thicket").

[194] Shapiro, *supra* note 17, at 120-21 (describing patent thicket as "a dense web of overlapping intellectual property rights" created by issuance of large numbers of patents to multiple firms).

[195] *See, e.g.*, SCM Corp. v. Xerox Corp., 645 F.2d 1195, 1197 (2d Cir. 1981) (holding that Xerox's patent thicket surrounding photocopying technology did not constitute antitrust violation).

with overlapping claims,[196] obscuring the overall scope of the patents in aggregate, and increasing the administrative and legal burden on potential challengers.[197] Patent law forbids patenting the same invention twice.[198] In addition, the nonobviousness requirement for patentability prevents small tweaks and insignificant, predictable changes to an invention from receiving the protection of a new patent.[199] However, a claim that might be obvious in light of a previous claim or patent might be saved by a terminal disclaimer.[200] By forgoing the additional exclusion period that would ordinarily stem from a later-filed application, the inventor does not unfairly extend their rights and can potentially capture claims they could have included in the original patent.[201] Thus, inventors can claim new tweaks to the invention and have an incentive to disclose new information related to the invention to the public.[202]

While this policy rationale prevents extension of the exclusivity period and allows a valuable mechanism by which inventors can capture additional claims, these terminal disclaimers allow companies to file a huge number of patents with similar or overlapping claims without fear of encountering obviousness issues related to their other patents.[203] Importantly, invalidation of the original patent that forced the subsequent patents to add terminal disclaimers does not result in the subsequent patents' automatic invalidation or unenforceability.[204] Thus, even though two patents may be linked by a terminal disclaimer, they must be invalidated separately, even if the invalidation arguments would be identical.[205] If one company obtains numerous patents this way, a challenger must invalidate each patent separately—increasing the burden of cutting through the patents and bringing a competing invention, or a biosimilar, to market.

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[196] Wu & Cheng, *supra* note 23, at 146-47 (describing a cluster of overlapping patents identified for one biologic, including two patents that used different language for identical amino acid sequence).

[197] *Id.* at 148-49 (explaining increased litigation and patent search costs associated with patent thickets).

[198] 35 U.S.C. § 101.

[199] *See supra* notes 109-12 and accompanying text.

[200] *See supra* Section I.E.

[201] *See* 37 C.F.R. § 1.321(b) (2021) ("An applicant may disclaim or dedicate to the public the entire term, or any terminal part of the term, of a patent to be granted."); MPEP, *supra* note 116, § 804.02 ("A rejection based on the statutory type of double patenting can be avoided by amending the conflicting claims so that they are not coextensive in scope.").

[202] *See* Wu & Cheng, *supra* note 23, at 175 (explaining that terminal disclaimer system was "initially designed to protect incremental improvements of the patented invention").

[203] *Id.* at 158-59 (describing multiple terminal disclaimer strategy for securing larger swath of patents).

[204] *See* MPEP, *supra* note 116, § 1490(IV) (describing process for processing statutory disclaimers).

[205] *See* Ortho Pharm. Corp. v. Smith, 959 F.2d 936, 941-42 (Fed. Cir. 1992) ("[T]he filing of a terminal disclaimer . . . raises neither presumption nor estoppel on the merits of the rejection." (quoting Quad Env't Techs. Corp. v. Union Sanitary Dist., 946 F.2d 870, 874 (Fed. Cir. 1991))).

Another reason firms can accrue large numbers of similar or overlapping patents is that the USPTO is understaffed and underfunded, resulting in examiners having a very brief period of time to analyze each patent.[206] Additionally, many of the patentability requirements entail detailed factual analyses, assessments of the prior art, and considerations of the knowledge of a person having ordinary skill in the art of the invention.[207] Given the time constraints, an examiner may not be able to consider every possible argument or find every piece of prior art. Inevitably, patents issue that should be rejected based on any of the numerous requirements for patentability.[208]

Ordinarily, the market can correct these mistakes and oversights through litigation: motivated competitors challenge the patent by identifying overlooked prior art and producing the strongest arguments against validity. However, as the number of patents in a firm's arsenal increases, the motivation of the competitors also must increase; invalidation of any one patent will not immediately allow competition, and suing over more patents inevitably increases the legal bill for even a successful suit. Thus, patent thickets can overwhelm the corrective effect of third-party litigation, resulting in potentially invalid patents running for an entire patent term.

Strategically, having a large number of patents deters potential biosimilar market entrants as the specter of extensive and expensive patent litigation looms large.[209] Even if the biologic patents are of questionable merit, invalidation of any one patent does little to free up the space when several more patents still cover the same technology. As a matter of simple cost-benefit analysis, the potential of encountering this resistance to biosimilar market entry increases the risk and cost associated with bringing these drugs to market; a firm may decide that it will be easier and cheaper to forgo a few years of revenue and allow some patents to expire rather than risking early entry and litigation.[210]

In addition, filing numerous patents may also allow the patent holders to extend the patent term beyond the expiration of the first patent of the drug, a process critically dubbed "evergreening."[211] Companies evergreen by filing numerous follow-on patents, making slight tweaks to the formulation or process that yield questionable therapeutic benefit over the original patents.[212] One way companies evergreen is through the use of continuation applications. As

[206] *See supra* note 112 and accompanying text.

[207] For example, nonobviousness requires these considerations. *See, e.g.*, Graham v. John Deere Co., 383 U.S. 1, 10-11 (1966).

[208] If every patent that issued was valid, patent litigators would have very few cases to pursue.

[209] *See* Nayak, *supra* note 30 (reporting that pharmaceutical patent cases with only $1-10 million at risk cost median of $2.5 million).

[210] *See* Hacohen, *supra* note 35, at 491-92 (describing difficulty in determining "the extent of [patents'] permissible exclusion without investing in costly and lengthy litigation").

[211] *See supra* notes 33-36 and accompanying text (describing evergreening).

[212] *See* Wu & Cheng, *supra* note 23, at 150-51.

discussed in Section I.E, continuation applications allow inventors to file additional patent claims for newly discovered features of their technology supported by the original disclosure.[213] However, like other aspects of the patent system, the process can be abused. Continuing to add new claims can keep an application eternally pending, effectively allowing multiple patent extensions.[214] Because continuation applications have a later filing date than the original application, these patents will also expire later than the original patent expires. Because these patents cover the same technology, the new patents effectively extend the exclusivity period for the underlying technology.

Although new claims without a terminal disclaimer are not supposed to be obvious, the USPTO is often underpowered to make these determinations during the relatively brief examination period.[215] Thus, many patents of questionable value issue.[216] While litigation and validity challenges exist as an ex post mechanism for defeating patents of questionable merit, when combined with the sheer volume of patents present in the patent thicket, drug manufacturers can overwhelm potential challengers and maintain their grip on the market.

Evergreening compounds the anticompetitive effects of the patent thicket by artificially extending the term of patent exclusivity. Instead of a thicket lasting for twenty years, evergreening allows the thicket to extend for years longer. In addition, evergreening undermines the policy underlying patent law: a grant of a temporary monopoly in exchange for public disclosure of the patented technology. Although monopolies are typically disfavored under antitrust law, the patent system provides a limited exception in order to promote this public disclosure. Evergreening goes against the spirit of this exchange, artificially extending the monopoly without providing additional disclosures worthy of the additional patents' anticompetitive effects.

Bringing a biologic from preclinical testing to market is an expensive and uncertain process.[217] Many drugs fail along the way,[218] and companies often

[213] 35 U.S.C. § 120 (describing benefit of earlier filing); *see supra* Section I.E.

[214] *See, e.g.*, *In re* Neurontin Antitrust Litig., No. 1:02-cv-01390, 2009 WL 2751029, at *19 (D.N.J. Aug. 28, 2009) (noting that company "filed unnecessary continuation applications, and abandoned an approved patent application in an attempt to obtain" additional exclusivity).

[215] Wu & Cheng, *supra* note 23, at 156-57 (listing possible reasons for USPTO granting patents that should not issue, including examiner workload, funding, and examiner competency).

[216] *Id.*

[217] *See supra* Section I.C (discussing complexity of biologic manufacturing).

[218] Daniel Seaton, *New Study Shows the Rate of Drug Approvals Lower than Previously Reported*, BIOTECHNOLOGY INNOVATION ORG. (Jan. 9, 2014), https://archive.bio.org/media/press-release/new-study-shows-rate-drug-approvals-lower-previously-reported-0 [https://perma.cc/YHT6-A7CH] (finding overall success rate of drugs moving through FDA process to approval to be approximately one in ten).

cannot accurately predict the odds of success of any particular candidate.[219] Unpredictability and high development costs make preserving the market for a drug all the more important; the profits from one successful drug cover the cost of the failures.[220] Thus, pharmaceutical companies have every incentive to pursue these aggressive patent strategies and preserve their market share, as coming across a new blockbuster drug to replace the expiring agent is by no means an easy prospect.

While sanctions exist for those who assert clearly baseless claims or file frivolous lawsuits,[221] the unpredictability of patent litigation and the relative difficulty of determining patent scope means that applying for and subsequently asserting many of these patents is completely legal. Therefore, the only drawback to forming these patent thickets is potential invalidation of some of the patents. When a company has hundreds of patents at their disposal, invalidation is hardly a disincentive.

Accordingly, some argue that patent thickets and evergreening are essential for preserving incentives for research and development of new drugs.[222] These proponents of the current system argue that neither patent exclusivity nor the exclusivity period included in the BPCIA or Hatch-Waxman Act give the companies enough time to gain regulatory approval and enjoy the rewards of market exclusivity long enough to recover their investment and produce enough profit to make the entire process worthwhile.[223] Thus, adopting strong protections over their blockbuster drugs, including patent thickets and

[219] *See, e.g.*, Standish Fleming, *Why Pharma Risk Is Inherently Unpredictable and Why It Matters*, FORBES (Nov. 6, 2018, 1:03 PM), https://www.forbes.com/sites/stanfleming/2018/11/06/inherently-unpredictable-why-pharma-has-an-innovation-crisis-and-how-to-fix-it/?sh=6641832778e9 (describing drug development process as unpredictable and results of drug development as "inherently unknowable").

[220] One study estimated research and development costs for successful drugs after accounting for costs of failed trials. Olivier J. Wouters, Martin McKee & Jeroen Luyten, *Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018*, 323 JAMA 844, 845 (2020). The estimated median research and development cost to bring a new drug to market after accounting for costs of failed trials was $985.3 million whereas the median cost without accounting for failed trials would only be $319.3 million. *See id.* at 849.

[221] *See, e.g.*, FED. R. CIV. P. 11 (describing standards and sanctions for nonfrivolous lawsuits).

[222] *See, e.g.*, Henry Grabowski, Genia Long & Richard Mortimer, *Data Exclusivity for Biologics*, 10 NATURE REVS. DRUG DISCOVERY 15, 16 (2011) ("[I]f biologic patents provide relatively strong protection with significant patent life remaining at approval, patents alone will be sufficient to maintain investment incentives . . . .").

[223] *See* Henry Grabowski, *Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REVS. DRUG DISCOVERY 479, 486-87 (2008) (estimating break-even period for new biologics between 12.9 and 16.2 years).

evergreening, is essential to ensure that their innovation is properly rewarded.[224] Finally, they argue that nothing legally prevents them from adopting these strategies.[225]

As discussed in Part I, biologics are substantially more complicated than small-molecule compounds, with critical structural features often determined by the manufacturing process. Accordingly, one would reasonably expect that a biologic may require more patents, especially process patents, than a much simpler small-molecule compound with a precise and well-delineated structure that often lends itself to one or a small number of composition of matter patents. In addition, the patents surrounding the biologic may be easier to invent around, as it may be easier to identify equivalent processes than substitute the precise active ingredient in small-molecule drugs.[226] Thus, a firm developing a biosimilar potentially has more opportunity to find equivalent, noninfringing processes than a firm working on a generic small-molecule drug. This means that a single biologic patent results in a smaller scope of protection than a single small-molecule patent.[227] As such, this argument for more aggressive patenting appears to extend to biosimilars. However, it falls flat in the face of the already narrow biologics market; because of the regulatory environment and the complexity of biologics, competition is already constrained. These intrinsic barriers to competition undermine the argument for allowing patent thickets and evergreening as additional artificial barriers to competition.

Patent thickets extend beyond the bounds of any reasonable increase in patenting attributable to the added complexity of biologic structure and manufacturing.[228] The increased importance of process patents also provides subject matter for additional patents; while it may be difficult to contemplate additional ways to patent a small molecule, duplicative patents on each stage of the biologic manufacturing process allow for more extensive thickets than could appear in the small-molecule context.[229] In addition, the fact that biosimilars need only be similar, not identical, means that the original biologic manufacturer can potentially block biosimilar competition by patenting related compounds

[224] *See* Hacohen, *supra* note 35, at 487 (noting how drug manufacturers argue that evergreening adds protection in a system "which is grossly insufficient to account for the costly and uncertain process of pharmaceutical development").

[225] *See id.* ("In [the] view [of proponents of evergreening], any additional exclusivity provided by the new patents rightfully complements preexisting legal protections for the old drug . . . .").

[226] *See* Wu & Cheng, *supra* note 23, at 155, 159.

[227] *See id.* at 155 ("Due to their larger size, and the existence of similar effective variants . . . . the scope of a single biologic patent is relatively smaller compared to that of a small-molecule patent." (footnote omitted)).

[228] *See id.* at 141 tbl.7 (determining that seventy-eight patents on Humira included overlapping claims and terminal disclaimers suggestive of double patenting).

[229] *See id.* at 159-60 (finding that almost half of patents on biologics were manufacture patents, while patents on small-molecule drugs did not include any manufacture patents).

and processes not directly used for manufacture of the original drug.[230] Even if the biologic manufacturer patents processes ultimately not employed by the prospective biosimilar manufacturer, the added burden of reviewing, working around, and potentially litigating these related patents increases the cost and difficulty of competition.

While pharmaceutical companies may rightly believe that their biologic research and development is under-rewarded under current law,[231] patent thickets and evergreening should not be the mechanism by which these companies secure additional compensation. Filing these patents creates a burden on the USPTO, muddies the boundaries and scope of legal protections surrounding the biologic, and discourages biosimilar competition. Additionally, these patents result in expensive and time-consuming litigation—funds that could instead be used to research new treatments deserving of their own patent protection. If statutory incentive periods are insufficient to properly reward biologic innovation in the pharmaceutical industry, then these companies should seek changes to patent law or to regulatory-granted exclusivity periods.[232] Artificially extending these periods through patenting and evergreening unfairly stifles already limited competition without explicit regulatory approval or oversight.

C. *Anticompetitive Biologic Patent Thicket Use*

While the characteristics of the biologic regulatory environment present several potential antitrust issues,[233] this Note focuses on those issues likely to arise from patent thickets. Discussed abstractly above, the broad anticompetitive harm from patent thickets is that they discourage or delay biosimilar market entry, make invalidity challenges massively expensive to the point of barely being economically feasible, and potentially extend the exclusivity period for the original biologic. The *Humira* litigation provides a concrete example of a patent thicket in action, demonstrating the anticompetitive effect a biologic patent thicket can have on prospective biosimilar market entrants. In addition to the passive deterrence from the sheer volume of patents thicket, AbbVie

[230] *See id.* at 160-63 (describing almost troll-like ability of biologic manufacturers to strategically patent to block biosimilars).

[231] *See* Eric Budish, Benjamin N. Roin & Heidi Williams, *Do Firms Underinvest in Long-Term Research? Evidence from Cancer Clinical Trials*, 105 AM. ECON. REV. 2044, 2045 (2015) (arguing that patent system provides "very little incentive" for long-term research because inventions that have long lag between invention and commercialization receive reduced patent term).

[232] *See, e.g.*, Robert D. Cooter & Uri Y. Hacohen, *Progress in the Useful Arts: Foundations of Patent Law in Growth Economics*, 22 YALE J.L. & TECH. 191, 214 (2020) (discussing longer exclusivity periods for pharmaceutical patents); Robin Feldman, *Regulatory Property: The New IP*, 40 COLUM. J.L. & ARTS 53, 64 (2016) (discussing regulatory exclusivities such as marketing rights).

[233] *See generally* Carrier & Minniti, *supra* note 59 (exploring multiple potential antitrust issues surrounding biologics and predicting likelihood of encountering them).

aggressively asserted their patent thicket before making settlement offers providing European-market access worth millions of dollars.[234] Unsurprisingly, manufacturers took the deal, leaving the U.S. market without direct Humira competition.[235]

An examination of the patents covering Humira reveal a particularly dense patent thicket. AbbVie, the patent holder, filed 247 patent applications related to Humira, of which 132 were granted.[236] Underscoring the notice issue of biologic patents, another analysis of Humira patents counted 154 total related patents.[237] Of these patents, at least nine clusters of highly similar patents exist.[238] For example, twenty-one of these patents claim some variation of the formulation for Humira; these patents all "belong to the same patent family and are all chained continuations of the same U.S. patent application."[239] The original application has since been abandoned,[240] possibly suggesting its use as a tool to produce these voluminous patent families. Analysis of the elements of the claims in this grouping show that all patents "claim nearly identical components" and "significantly overlap with one another."[241] Analysis of the timing of Humira patents show an original patent filed in 1996, six years before Humira's U.S. market entry.[242] Before market entry, Humira had relatively few patents; AbbVie filed the vast majority of patents beginning in 2010.[243] As a result, the final Humira patents will not expire until 2034, almost forty years after the first Humira patent.[244] These patterns are not unique to Humira or AbbVie—other biologics have similarly large numbers of patents over a period of years.[245]

Securing a patent thicket provides passive defense from competition by discouraging suits; only highly motivated litigants with strong arguments would consider going up against so many patents. Because of the overlapping nature of the claims and the uncertain legal scope of the overall thicket, competitors are deterred from potentially entering the market and attempting to compete with

[234] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 825 (N.D. Ill. 2020).

[235] *Id.*

[236] *Id.* at 822.

[237] *See* Wu & Cheng, *supra* note 23, at 129-30 (noting additionally that, of the drugs analyzed, the two drugs with highest patent counts were both biologics).

[238] *Id.* at 141 tbl.7.

[239] *Id.* at 143 (footnote omitted).

[240] *See id.* at 143 n.194 (noting that U.S. Patent Application No. 10/222,140, filed on August 16, 2002, is now abandoned).

[241] *Id.* at 146.

[242] *Id.* at 132 fig.9.

[243] *See id.* (displaying history of AbbVie's Humira patents); *see also In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 822 (N.D. Ill. 2020) (describing how AbbVie began applying for Humira-related patents in lead up to expiration of parent patent).

[244] *See* Wu & Cheng, *supra* note 23, at 132 fig.9 (displaying Humira's active patent counts by year).

[245] *See id.* at 133 fig.11 (displaying Rituxan's active patent counts by year).

the biologic. Thus, merely assembling the patent thicket inhibits competition and should constitute an antitrust violation.

AbbVie's actions demonstrate that patent thickets can be used offensively as well. Although Humira entered the market in 2002, the vast majority of Humira patents issued in 2014 or later.[246] The plaintiffs in the suit argued that many of these patents were invalid and should not have issued in the first place.[247] As biosimilar manufacturers sought to enter the market, AbbVie aggressively asserted its patents during the patent dance.[248] Some of the patent claims appeared to be baseless, "for which there was not even an arguable claim of infringement."[249] Although the manufacturers believed that most patents were invalid, and some began the litigation process, the manufacturers ultimately entered settlement agreements to avoid burdensome litigation.[250] The plaintiffs in the case alleged that this aggressive assertion of patents with dubious merit and enforceability unfairly defeated the biosimilar approval and marketing process, delayed biosimilar market entry, and prevented any real challenges to their patents, extending AbbVie's monopoly over the market.[251]

This aggressive assertion of patents does not have to be isolated to Humira; any biosimilar patent thicket would allow similar tactics. Companies have every incentive to assert every patent with a colorable infringement argument against a prospective biosimilar. Without a prior notice requirement, the patent dance is the prospective biosimilar's first encounter with the asserted patents. Because the manufacturer has already developed their product and process, surprise patents could be particularly costly or damning. Thus, this aggressive patent assertion inhibits the competition the BPCIA is designed to foster and should constitute an antitrust violation.

Because of the high investment costs associated with developing a biosimilar, potential competition with biologics is already limited. Combined with the likely aggressive assertion of patents during the patent dance, biosimilar producers face the prospect of prolonged litigation before breaking into the market and recovering their development costs. Suddenly, the company asserting the infringement claims offers the chance to settle. Rather than demanding payment, like one might expect from a company alleging patent infringement, the company instead offers the chance to begin marketing the biosimilar in another market, an opportunity worth hundreds of millions of dollars. The choice is between expensive litigation or millions in revenue—it is not hard to see why companies accept the settlement agreement.

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[246] *In re Humira*, 465 F. Supp. 3d at 822 ("More than 90% of [Humira] patents were issued in 2014 or later, despite the fact that Humira was first marketed in 2002.").

[247] *See id.* at 823 ("[P]laintiffs say they can quickly identify whole swaths of AbbVie's IP portfolio that should not have issued.").

[248] *See id.* at 832-33.

[249] *Id.* at 825.

[250] *Id.* at 824.

[251] *Id.* at 827.

This scenario played out exactly in the *Humira* litigation: the end result of AbbVie's aggressive patent assertion was settlements with each of the hopeful biologics manufacturers, delaying U.S. biosimilar launches until 2023 while allowing earlier entry into European markets.[252] The plaintiffs in the suit alleged that AbbVie had negotiated "reverse payment" deals, granting access to lucrative European markets in exchange for continued monopoly control of the most valuable market in the world, the United States.[253] Agreeing to allow entry into the European market granted the biosimilar manufacturers the chance to begin bringing in revenue to cover the high costs for developing the biosimilars.

Faced with the uncertain prospects of continued litigation in the United States, accepting the rights to begin commercializing their products in Europe proved to be too profitable to resist. Accordingly, the United States was left stuck with substantially higher costs and no Humira competition.[254] The plaintiffs alleged that, although the settlements did not amount to explicit payments for delayed entry, granting European entry rights effectively divvied up the market for Humira and paid off the biosimilar manufacturers with lucrative market entry.[255] Because of the misaligned interests between biosimilar manufacturers and patients, biosimilar manufacturers consider only their profits when considering these deals, not the potential patient and consumer welfare benefits of increased competition in the United States.[256]

The idea of paying a potential competitor not to compete is not a new concept, and antitrust law specifically prohibits these naked anticompetitive payments.[257] Despite courts' generally favorable view of settlements, a settlement preventing competition essentially transfers the benefits consumers would derive from competition to the monopolist, who can then use a portion of this gain to pay the competitor.[258] Here, this market divvying is not a naked payment; other biologic manufacturers could very easily employ similarly structured deals. For patients,

[252] *Id.* at 824.

[253] *Id.* at 825 (describing how AbbVie used European entry dates as bargaining chips over entry dates for United States during negotiations).

[254] *See* Rowland, *supra* note 10 ("With no competition, AbbVie has a free hand to boost prices in the United States for another three years.").

[255] *In re Humira*, 465 F. Supp. 3d at 836.

[256] Amici Curiae Brief of 66 Law, Economics, Business, and Medical Professors in Support of Plaintiffs-Appellants at 3, UFCW Loc. 1500 Welfare Fund v. AbbVie Inc., No. 20-2402 (7th Cir. Oct. 9, 2020) [hereinafter Amici Curiae Brief of 66 Professors] (noting that AbbVie's behavior was "a windfall for the biosimilar competitors paid off with some of the bounty" but a "tragedy for consumers" unable to pay for treatment).

[257] *See* FTC v. Actavis, Inc., 570 U.S. 136, 157-60 (2013) (finding that reverse payments, when large and unjustified, "outweigh the . . . desirability of settlements" and violate antitrust law).

[258] *See* Amici Curiae Brief of 66 Professors, *supra* note 256, at 9-10 (explaining that, while two parties to antitrust litigation may benefit from settlement, it can be at expense of consumers forced to pay monopoly prices).

unfortunately, the structure of the deal matters little when the end result is continued monopoly prices and limited treatment options.

The temptation to accept these settlement agreements underscores the misaligned interests of patients and biosimilar manufacturers: lower drug prices and increased competition are by-products of biosimilar market entry, not a goal of the manufacturers. In fact, biosimilar manufacturers have other incentives to accept a market-divvying settlement agreement as well: by receiving a license to compete in another market, the manufacturers need not litigate the patent protection in that market. This leaves the potentially disputed patents in force, preventing other biosimilar manufacturers from entering the market unless they litigate the patents or work out a similar settlement agreement. Thus, the original manufacturer's patent thicket now serves to protect the chosen biosimilar too. By continuing to restrict potential market entrants, prices can remain higher than if other firms were able to compete. Therefore, these reverse settlement agreements restrain competition in an already narrow market and should be antitrust violations.

III. CUTTING THROUGH THE THICKET: ANTITRUST SOLUTIONS TO PATENT THICKET MISUSE

Both BPCIA regulation and patent law contribute to the unique harm caused by patent thickets protecting biologics. Accordingly, changes to either regime may help alleviate some of the harms of the patent-thicketing process. However, changes to patent law affect patents in all industries unless unwieldy, biosimilar-specific carve outs are adopted. In addition, changes to the BPCIA are probably not best equipped to counter practices firmly grounded in patent law. While fine-tuned legislative tinkering may help counter some harms, and is by no means discouraged by this Note, antitrust law offers the potential to broadly smack down anticompetitive behavior surrounding biosimilar patent thicket acquisition and abuse. In addition, successful use of antitrust principles would have a deterrent effect. Although how much any one case would deter others depends on the facts of the case, the prospect of antitrust scrutiny could certainly discourage some of the worst abuses.

This Part will examine how antitrust doctrines could be used to combat the anticompetitive effects of patent thickets discussed in Part II. Although the district court in the *Humira* litigation did not agree with the plaintiffs' antitrust allegations, Section III.A will explore how obtaining the patent thicket and subsequently asserting a broad range of questionable patents could constitute antitrust violations. Section III.B will discuss the antitrust implications of reverse settlement agreements. Finally, Section III.C will suggest that FTC enforcement of the antitrust theories described would be superior and have a higher likelihood of success than private litigation.

A. *Aggressive Patent Assertion to Maintain a Wrongful Monopoly*

As discussed in Part II, biologic manufacturers obtain broad swaths of patents to protect their lucrative blockbuster drugs, making competition difficult or impossible. Some of these patents are tied together with terminal disclaimers, resulting in significant overlap and questionable nonobviousness arguments.[259] Companies then assert this thicket against prospective biosimilar manufacturers, delaying entry and encouraging settlement.[260] These actions seem anticompetitive on their face, but could they constitute antitrust violations?

As described in Section I.F, to allege a section 2 claim, a plaintiff must show: "(1) the possession of monopoly power in the relevant market and (2) the willful acquisition or maintenance of that power as distinguished from growth or development as a consequence of a superior product, business acumen, or historic accident."[261] In the context of patent thickets and biosimilars, the first element will frequently be an easy burden for a challenger because the biologic manufacturer will necessarily have a monopoly over the product and the market if they are using a patent thicket to keep out biosimilars.[262] The second element, however, will prove more difficult. To overcome the *Noerr-Pennington* doctrine immunizing lawful government petitioning from antitrust scrutiny,[263] biosimilar manufacturers would have to show that acquiring the patent thicket and then aggressively asserting it during litigation crossed from permitted competitive business practice to fraudulent, sham abuse of process.[264] Despite this potential difficulty, the anticompetitive harm from patent thickets, coupled with the already narrow competitive market for biologics, make antitrust enforcement

[259] *See supra* Section II.B (discussing terminal disclaimers).

[260] *See supra* Section II.C (discussing biologic manufacturers' aggressive use of patent thickets); *see also* Wu & Cheng, *supra* note 23, at 148 ("One of the most eminent capabilities of patent thickets is the leverage it provides for patent owners to force generics or biosimilar manufacturers into settlements.").

[261] United States v. Grinnell Corp., 384 U.S. 563, 570-71 (1966).

[262] The more treatment substitutes that exist for the particular biologic in question, the weaker this argument becomes. *See id.* (explaining that substitute products must be considered when determining "relevant market" because "commodities reasonably interchangeable make up that 'part' of trade or commerce which § 2 protects against monopoly power"). As discussed previously, however, biologic drugs tend not to have many effective substitutes and often improve dramatically over the previous standard of care. *See supra* text accompanying notes 167-75 (discussing reasons for lack of effective substitutes in biologic market). In addition, the broad scope of the patents may prevent a swath of similar drugs that could potentially compete, leaving the biologic manufacturer with the entire market. *See* Wu & Cheng, *supra* note 23, at 149 (arguing that patent thickets provide "multiple patent lives" to a drug and therefore "result[] in a lower possibility for the drug's biosimilar or generic to be commercialized").

[263] *See In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 828 (N.D. Ill. 2020).

[264] *See* Wu & Cheng, *supra* note 23, at 171 (noting element difficult to establish because courts have been reluctant "to penalize monopolists that engage in normal competitive behavior").

one of the last lines of defense for increasing competition and improving patient and consumer welfare.

1. Obtaining the Patents

First, litigants could focus on acquiring the patent thicket as an anticompetitive practice. As discussed in Part II, one way to form patent thickets is by tying together large volumes of patents with terminal disclaimers to avoid nonobviousness issues.[265] While patent law permits this terminal disclaimer and continuation practice,[266] courts should consider these actions in the broader context of biologic market preservation. If a court finds overwhelming overlap between patents and a high volume of near duplicative specifications and claims, a court should not need to dive very deeply into the science to appreciate the filing as an anticompetitive tactic. In the small-molecule context, courts have imposed antitrust sanctions for abusive use of continuation applications.[267] There, the manufacturer strategically used the continuation process to delay patent issuance, which allowed the company to obtain multiple thirty-month stays from the FDA and delay generic competition longer than intended by the Hatch-Waxman Act.[268]

Although the BPCIA does not include a stay provision comparable to the Hatch-Waxman Act, biologic manufacturers appear to be manipulating the continuation process for similar anticompetitive effects. The patents covering Humira, for example, contain large clusters of patents that stem from the same application, which was subsequently abandoned after numerous related patents issued.[269] Viewed individually, a court may be reluctant to criticize any one continuation application.[270] Viewed collectively, however, a court should be able to appreciate the sharp distinction between legitimately claiming new tweaks to an invention and padding a patent thicket.

Biologics manufacturers would likely argue that the higher volume of patents is due to the complexity of these large-molecule compounds.[271] Further, they

[265] *See supra* notes 195-202 and accompanying text (discussing why manufacturers create patent thickets and problematic purposes patent thickets serve).

[266] *See supra* notes 198-203 and accompanying text (explaining policy rationale behind terminal disclaimers but warning against consequences of misuse).

[267] *See, e.g.*, *In re* Neurontin Antitrust Litig., No. 1:02-cv-01390, 2009 WL 2751029, at *19 (D.N.J. Aug. 28, 2009) (holding that monopolization scheme, if proven, is sufficient to warrant exception to *Noerr-Pennington* immunity).

[268] *Id.* at *18-20.

[269] *See* Wu & Cheng, *supra* note 23, at 143 (noting that patents in Humira's "'583 Type II Patent Thicket" belong to same patent family, are continuations of same application, and have nearly identical specifications).

[270] *See, e.g.*, *id.* at 165 (explaining that courts' reluctance stems from fact that "the line of what accumulates to a patent thicket is unclear").

[271] *See, e.g.*, *id.* at 155-56 ("[B]iologic companies have even more motivation to file more patents to compensate for the fact that one or a few patents will not fully cover the different 'aspects' of the biologic.").

would likely argue that even if the overlapping patents were improper, many of the patents in the thicket were legitimate and should not be scrutinized because of the arguments against another group of patents.[272] Accordingly, plaintiffs would have to show that the continuation practice was so abusive that it should similarly infect the patents unrelated to these families.[273] Courts have previously reasoned that inequitable conduct for one patent claim could infect other claims within the same patent,[274] but courts have been reluctant to expand this reasoning across patents.[275] This reluctance likely contributes to the incentives for companies to file multiple patents rather than just multiple claims.

The burden on plaintiffs to show that all patents were affected by these abusive practices is a high one, and plaintiffs may be forced to focus on just the continuation applications.[276] For example, in the *Humira* litigation, the district court looked at the rate of AbbVie's patent application approvals and noted that "more than half (53.4%) of AbbVie's patent applications resulted in patents."[277] The district court used this figure to satisfy itself that the patents that did issue were not objectively baseless.[278] Here, the district court granted great deference to AbbVie in determining what conduct was improper and what conduct was lawful petitioning, reasoning that the balance of the activity weighed in AbbVie's favor, even at this early stage in the litigation.[279] To recalibrate this balance, increasing scrutiny on double patenting and patent families with broader claims could make the process of acquiring a patent thicket explicitly anticompetitive. This may serve both as a deterrent for acquiring the thicket in

[272] *See id.* at 166 (noting that "unclean hands defense" is difficult to assert with patent thickets because "[t]he simple act of applying for and receiving a patent, standing alone, can hardly be the basis for patent invalidation" (alteration in original)).

[273] *Id.* at 172 (opining Humira litigation plaintiffs would have had better chance proving willful monopoly power by emphasizing "that the patents covering Humira are overlapping, non-inventive, or . . . obtained through fraudulent conduct, if possible").

[274] *See, e.g.*, Kingsdown Med. Consultants, Ltd. v. Hollister Inc., 863 F.2d 867, 877 (Fed. Cir. 1988) ("When a court has finally determined that inequitable conduct occurred in relation to one or more claims during prosecution of the patent application, the entire patent is rendered unenforceable.").

[275] *See, e.g.*, Pharmacia Corp. v. Par Pharm., Inc., 417 F.3d 1369, 1375 (Fed. Cir. 2005) (declining to extend inequitable conduct in one patent to second patent not acquired through same culpable conduct).

[276] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 830 (N.D. Ill. 2020) (noting it is not enough for plaintiffs to merely "describe 'numerous flaws in AbbVie's patents and its assertion of them'" (quoting Plaintiffs Opposition to Defendants' Motion to Dismiss at 22, *In re Humira*, 465 F. Supp. 3d 811 (N.D. Ill. 2020) (No. 1:19-cv-01873))).

[277] *Id.*

[278] *Id.* ("Even in circuits that apply the type of more flexible test plaintiffs say should be applied here, a batting average of .534 would be too high to plausibly allege sham petitioning as a matter of law.").

[279] *Id.* at 831 (finding AbbVie's petitioning protected by *Noerr-Pennington* due to overall high success rate despite Patent Trial and Appeal Board invalidating three of five patents during inter partes review).

the first place, as well as an ex post mechanism for ensuring that the "sharp elbows" of the biologics manufacturers do not block others from entering the market.[280]

2. Asserting the Patents

Despite the challenges to bringing antitrust claims based solely on the process of obtaining the patent thicket, these actions, coupled with aggressive assertion of the thicket, are more likely to draw antitrust sanctions. Like the process of filing patents, litigating legitimate claims is protected by the *Noerr-Pennington* Doctrine.[281] However, "'a pattern of baseless, repetitive claims' instituted 'without probable cause, and regardless of the merits' falls outside of *Noerr–Pennington* protection."[282] The requirement for baseless claims is a difficult one to overcome;[283] patent validity is notoriously unpredictable, so it would be relatively simple for a biologics manufacturer to argue that it believes its patent valid and infringed. However, the patent dance process, including selecting which claims to assert, is not yet petitioning the government or litigation, suggesting that antitrust scrutiny at this stage may not be subject to the objectively baseless requirement.[284] In addition, manufacturers may go too far in the patent dance; in an effort to unleash their entire patent arsenal, manufacturers may assert claims during the patent dance for which they cannot make a colorable infringement argument.[285]

For example, in the *Humira* litigation, AbbVie asserted sixty-six patents against one manufacturer and refused to respond to the manufacturer's disputed patents;[286] AbbVie also asserted several patents against another manufacturer

[280] *Cf. id.* at 834 (finding that vast majority of alleged scheme is "immunized from antitrust scrutiny, and what's left are a few sharp elbows thrown at sophisticated competitors participating in regulated patent and biologic-drug regimes").

[281] *In re* Neurontin Antitrust Litig., No. 1:02-cv-01390, 2009 WL 2751029, at *17 (D.N.J. Aug. 28, 2009) (noting *Noerr-Pennington* doctrine, which protects "activities by parties to influence government policy or legislation from antitrust claims," has been expanded "to include litigation to protect rights such as patents").

[282] *In re Humira*, 465 F. Supp. 3d at 828 (quoting Cal. Motor Transp. Co. v. Trucking Unlimited, 404 U.S. 508, 513 (1972)).

[283] Wu & Cheng, *supra* note 23, at 171 (noting act of being litigious not necessarily a sham so long as plausible arguments on which patent owners could have prevailed existed in suit).

[284] *See In re Humira*, 465 F. Supp. 3d at 832 n.14 (noting that exchanges during patent dance might not qualify as petitioning because "neither party is (at that moment) asking the government to do anything"); *see also* Freeman v. Lasky, Haas & Cohler, 410 F.3d 1180, 1184 (9th Cir. 2005) (explaining that "discovery is merely communication between parties as an aid to litigation" and is not petitioning because it is not "in any sense a communication to the court").

[285] Plaintiffs allege this happened in the *Humira* litigation. *See In re Humira*, 465 F. Supp. 3d at 832 (describing how plaintiffs accused AbbVie of "objectively baseless petitioning" during the patent dances).

[286] *Id.*

that were not used in Humira or the prospective biosimilar.[287] This pattern of aggressive assertion parallels the strategy of aggressive prosecution; after acquiring all of these patents, the temptation is to use them to your advantage. While the parties are supposed to negotiate during the dance in good faith, a biologics manufacturer has little incentive to be conservative in selecting patents. Antitrust scrutiny for asserting objectively baseless claims, especially when combined with obtaining a patent thicket, would provide that incentive. Biologics manufacturers select the patents they will assert during the dance, so applying this scrutiny could prevent the worst patents from being litigated. By filtering out the weakest patents, the total number of asserted claims would fall, reducing biosimilar manufacturers' legal burden and alleviating some of the effects of patent thickets. AbbVie's approach to the patent dance, where several asserted patents were baselessly asserted, should draw antitrust scrutiny, at least enough to survive a motion to dismiss.

In the small-molecule context, courts have imposed antitrust sanctions for "use of overbroad listing codes in the Orange Book that were not limited to exclude a generic's noninfringing use."[288] Without an Orange Book process under the BPCIA, selecting and asserting an overbroad portfolio of patents most directly parallels this anticompetitive activity, in both cases designed to keep competitor drugs from entering the market.[289] The FDA's ministerial role in maintaining the Orange Book does not supply the FDA with enough power to prevent anticompetitive abuses of the regulatory process,[290] necessitating a role for antitrust law. In the biosimilar context, the FDA does not even have this minor role in looking over the patents related to biosimilar approval, suggesting that antitrust scrutiny in this context is even more vital.[291]

As mentioned above, showing that the eventual patent lawsuits are objectively baseless is more difficult, as "[a]ny lawsuit 'reasonably calculated to elicit a favorable outcome' is objectively reasonable, and any 'successful action self-proves its reasonableness.'"[292] In the *Humira* litigation, the district court relied on the success figures from inter partes review proceedings to reason that AbbVie's assertion of patents was not objectively baseless.[293] In addition, although the litigation never reached a conclusion on validity, the district court

[287] *Id.*

[288] Carrier & Minniti, *supra* note 59, at 36.

[289] *See id.* at 38 (suggesting that biologic manufacturers use "patent-prosecution tools to thwart biosimilar competition").

[290] *See id.* at 36 (arguing that fraudulent patent listings are evidence that Hatch-Waxman not effectively enforced, and therefore antitrust law "must fill the void").

[291] *See id.* at 18 ("[I]n contrast to the Hatch-Waxman Act, the BPCIA's patent resolution provisions are centered on private negotiation between the parties.").

[292] *In re Humira*, 465 F. Supp. 3d at 829 (quoting P.R. Tel. Co. v. San Juan Cable LLC, 874 F.3d 767, 769 (1st Cir. 2017)).

[293] *Id.* at 831 ("AbbVie's success rate during *inter partes* review was even higher, and establishes that AbbVie's conduct there was not objectively baseless, either.").

reasoned that the high approval rate of AbbVie's patent applications suggests some patents were legitimate.[294] The district court, relying on the fact that the claims settled, concluded that they were not objectively baseless, as the settlements involved concessions from both sides.[295] Unfortunately, by using this reasoning, the district court forgets that "[t]here is a risk that by focusing only on each individual action in a series, a broader pattern of anticompetitive conduct might escape policing and remedy."[296]

Biologics manufacturers will undoubtedly have valid patents protecting their drugs, and these patents should be enforced and litigated under the procedures set out in the BPCIA. But allowing the possibility of legitimate claims to overwhelm clear indications of anticompetitive behavior disservices biosimilar manufacturers and patients. Further, using patent approval rates as a proxy for the likelihood of patent litigation claims succeeding is unfounded, as numerous issued patents are later declared invalid after litigation. Finally, using settlement as a predictor of success may make sense in other contexts, but where few biosimilars can potentially compete and the settlements are structured as payments,[297] settlements may be more indicative of further anticompetitive activities than of strong patent claims.

B. *Settlements and Market Allocation*

While patent thickets are not essential for obtaining the anticompetitive settlements described in Part II, the increased leverage they provide makes these settlements more likely. Coupled with the limited competition inherent in the biosimilar market and with the high biosimilar development costs, the biologics market appears to be particularly vulnerable to this enhanced leverage—and presents an opportunity for antitrust sanctions to deter and correct abuses.

As discussed in Part I.F, reverse payment schemes can be subject to antitrust scrutiny under *Actavis*. One challenge when examining biosimilar settlements will be identifying whether there was a payment.[298] After *Actavis*, biologic manufacturers are unlikely to make naked payments for fear of antitrust sanctions, and may be more likely to engage in negotiations like AbbVie in the

[294] *Id.* (stating that AbbVie's 72.2% success rate "renders implausible" that AbbVie's submissions were objectively baseless).

[295] *Id.* at 833 ("When a lawsuit terminates in a settlement that provides substantial value to an antitrust defendant accused of initiating that lawsuit as a sham, that lawsuit is objectively reasonable.").

[296] *Id.*

[297] *See infra* Section III.B (explaining how courts determine whether settlement is subject to antitrust scrutiny).

[298] In *FTC v. Actavis, Inc.*, 570 U.S. 136, 147 (2013), the parties agreed to a settlement that ended litigation over the validity of the defendant's patent. While Actavis tried to frame this transfer as strictly a settlement, the FTC framed this settlement as a payment, arguing "that in substance, the plaintiff agreed to pay the defendants many millions of dollars to stay out of its market, even though the defendants did not have any claim that the plaintiff was liable to them for damages." *Id.* at 147-48.

Humira litigation, offering up early access to another market in exchange for prolonged exclusivity in the U.S. market.[299] However, the Supreme Court in *Actavis* emphasized that the focus should be on substance rather than form.[300] Other cases support this proposition as well.[301] An agreement that effectively pays the only motivated competition not to enter the U.S. market should be highly suspect.

In examining an alleged reverse payment, "the court should consider . . . whether the biologic manufacturer conveys 'a type of consideration not available as a direct consequence of winning the lawsuit.'"[302] Thus, patent-split agreements, where companies divide up the remaining exclusivity period, may not violate antitrust principles.[303] Similarly, allowing early entry in one region of the United States but not others may not create an antitrust issue.[304] However, the biologics most likely to be protected by aggressive patent thickets are the worldwide blockbuster drugs. U.S. patents protect drugs only in the United States. Therefore, neither winning a patent infringement case against a biologic manufacturer, nor showing that the allegedly infringed patent was invalid, would provide access to a foreign market subject to a completely different jurisdiction. Thus, an agreement granting access to a foreign market could constitute a payment under *Actavis*.

Further, the size of the payment is an important indicator of its propriety. A larger payment suggests weaker patents, or at least less confidence in the patent litigation.[305] Thus, a larger payment will be more suggestive of an anticompetitive reverse payment settlement. Payments that are "no more than a rough approximation of the litigation expenses saved through the settlement" are

[299] *See In re Humira*, 465 F. Supp. 3d at 824-25 (detailing how AbbVie reached settlement agreements involving European-market entry with nine manufacturers seeking to market biosimilars).

[300] *See* Amici Curiae Brief of 66 Professors, *supra* note 256, at 17 (explaining that antitrust analysis is "based upon demonstrable economic effect" of transaction (quoting Continental T.V., Inc. v. GTE Sylvania Inc., 433 U.S. 36, 59 (1977)).

[301] *See, e.g.*, King Drug Co. of Florence v. Smithkline Beecham Corp., 791 F.3d 388, 403 (3d Cir. 2015) (extending *Actavis* and finding agreement, which involved large transfer of value, subject to antitrust scrutiny); FTC v. AbbVie Inc., 976 F.3d 327, 356 (3d Cir. 2020) ("[W]e read *Actavis* . . . to apply to potentially anticompetitive reverse payments regardless of their form.").

[302] Carrier & Minniti, *supra* note 59, at 25 (quoting Michael A. Carrier, *Payment After* Actavis, 100 IOWA L. REV. 7, 9 (2014)).

[303] *Id.* at 24-25 (explaining no antitrust violation when agreement divides remaining patent term because entry date compromise reflects odds of success in litigation).

[304] Asahi Glass Co. v. Pentech Pharms., Inc., 289 F. Supp. 2d 986, 992-93 (N.D. Ill. 2003) (finding no antitrust violation where settlement temporarily confined company to Puerto Rican market and led to increased competition).

[305] *See* FTC v. Actavis, Inc., 570 U.S. 136, 158 (2013) ("[T]he size of the unexplained reverse payment can provide a workable surrogate for a patent's weakness, all without forcing a court to conduct a detailed exploration of the validity of the patent itself.").

more likely to be legitimate.[306] Here, biologic producers with patent thickets may actually have an advantage: the sheer volume of their patents increases the likely expense of the litigation needed to remove the barrier, increasing the potential payout of the settlement without violating antitrust rules. However, even expensive litigation may not be able to outweigh the potential payout from granting access to other markets. In fact, one would expect this opportunity would have to be greater in order to entice settlement rather than allow continued litigation. Thus, granting access to a foreign market may be large enough to trigger antitrust scrutiny.

The district court considering the *Humira* litigation drew several distinctions from *Actavis*-style reverse payments. To begin, more than one biosimilar manufacturer gained entry to the European market.[307] In addition, the district court concluded "[t]he transfer of value, as large as it was, did not have the hallmarks of an unjustified and otherwise inexplicable payment because the package either increased competition or preserved an anticompetitive status quo."[308] "[W]hen AbbVie agreed to let Amgen, Sandoz, and Samsung Bioepis enter the European and U.S. markets earlier than they might have been able to otherwise, consumers won and the market for Humira (and its generics) became more competitive."[309]

Here, the district court seems to place very little emphasis on the value the biosimilar manufacturers derive from a market-allocating settlement. Although not a mere cash payment, access to the European market provides a lucrative revenue stream. Facing a similar patent thicket in European jurisdictions, this settlement provided immediate access with no risk of further expensive litigation. Further, this European market access could not possibly have resulted from the litigation. Although the district court reasoned that allowing competition in Europe made the Humira market more competitive, the U.S. market became decidedly less competitive. Firms capable of developing biosimilars are already limited compared to generic manufacturers—now, several of the firms most motivated to attack the thicket have agreed to bow out. The patent system relies on third parties to police the validity of patents—by effectively paying off the motivated and advanced-stage biosimilar producers, an already astonishingly small number, who remains to challenge the thicket?

An outright ban of these settlements, even if just in the contexts of biologics, would be one way to prevent this particular patent thicket misuse. But specifically banning one form might allow a different form to emerge, accomplishing similar anticompetitive arrangements. It is likely no coincidence that the settlement agreements did not offer direct payments to the biosimilar

[306] *Id.* at 156-58.

[307] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 840 (N.D. Ill. 2020).

[308] *Id.* at 841.

[309] *Id.*

manufacturers, an arrangement harshly repudiated in *Actavis*.[310] Instead, considering agreements like this as evidence of anticompetitive activity seems more effective: courts are best equipped to weigh the terms of these agreements and examine their overall effect. A formal, bright line rule would be too easy to avoid. Acknowledging these settlements as reverse payment schemes that violate antitrust laws would remove one of the potential harms arising from patent thicket misuse.

C. *Government Agency Antitrust Enforcement*

As explained in Section I.F, antitrust enforcement can stem from either government or private action.[311] Private plaintiffs bringing antitrust actions must demonstrate how they suffered antitrust injury from the monopolists' actions, a showing that requires a detailed causation analysis.[312] In contrast, the DOJ or FTC must demonstrate only the antitrust violation; no causal nexus need be shown.[313] Because of the misaligned interests of biosimilar manufacturers and patients, coupled with the difficulties of demonstrating this causal link between forming and using patent thickets and antitrust injury, FTC enforcement may be the most promising way to successfully enforce antitrust law and limit the anticompetitive use of patent thickets. Historically, the FTC and DOJ have let private litigants drive the bulk of antitrust enforcement.[314] However, a new administration and an increasing scrutiny of monopoly power could increase the enforcers' willingness to expand their antitrust focus to biologic patent thickets.[315]

The plaintiffs in the *Humira* litigation were indirect purchasers of Humira: cities, insurance trust funds, and employee welfare benefit plans.[316] Plaintiffs alleged that they suffered an antitrust injury of monopoly pricing, explaining that but for the creation and anticompetitive use of the patent thicket, biosimilar competition would have decreased drug prices.[317] The plaintiffs argued that if

[310] *See Actavis*, 570 U.S. at 138 ("Payment for staying out of the market keeps prices at patentee-set levels and divides the benefit between the patentee and the challenger, while the consumer loses.").

[311] *See supra* notes 150-60 and accompanying text.

[312] *See supra* notes 152-54 and accompanying text.

[313] *See supra* notes 156-60 and accompanying text.

[314] *See, e.g.*, Rory Van Loo, *In Defense of Breakups: Administering a "Radical" Remedy*, 105 CORNELL L. REV. 1955, 1981 (2020) (pointing out that FTC orders only ten divestitures each year compared to thousands of private divestitures that occur annually).

[315] *See* Justin Danilewitz & James Morsch, *Significant Changes to the Antitrust Laws May Be Coming*, JD SUPRA (Feb. 26, 2021), https://www.jdsupra.com/legalnews/significant-changes-to-the-antitrust-8707551/ [https://perma.cc/5XSM-4YF3] (describing increased congressional and administrative interest in antitrust enforcement as well as new legislative proposals to expand power and funding for FTC).

[316] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 820 (N.D. Ill. 2020).

[317] *See id.* at 843 (noting that allegations satisfy first part of causation test because "[h]igher prices are one of the 'principles vices' [sic] proscribed by the antitrust laws").

the biosimilar manufacturers had pursued their invalidity arguments, they could have entered the market sooner than under the settlement agreements and decreased the drug's price.[318] The district court struck down this argument, reasoning that merely speculating that prices might go down is not enough to satisfy the causation analysis.[319] If litigation had proceeded, some patents may have been valid and prevented market entry until the same date as agreed in the settlement.[320] Therefore, the district court reasoned, a clear path to lower prices was not present. Further, even if the patents had all been invalid, the amount of time to reach that conclusion might still have resulted in the same delay.[321]

The district court's logic demonstrates the difficulty private plaintiffs will encounter in challenging patent thickets and collusive settlements. Because the extensive patent thicket on its face extends beyond the period in which the biosimilar manufacturers seek to enter the market, it will be difficult to demonstrate that but for the thicket, prices would have fallen. If even one patent is valid and would be infringed by a biosimilar, then no competitor could enter during the period of that patent and drive down prices.[322] Part of this difficulty may stem from courts' tendency to grant great deference to patents, even if the patent has a fair chance of being invalid. This formulation of the causation standard seems impossibly rigid; it would be very difficult for the plaintiffs to ever show what would have happened if the litigation had proceeded without actually litigating the patents.[323] Using this logic, it would be very difficult to ever show reverse payment antitrust violations under *Actavis*,[324] which suggested that "it is normally not necessary to litigate patent validity" for the purposes of an antitrust suit.[325]

One way to avoid this limiting causation analysis entirely would be to encourage the FTC to bring these suits. Tasked with protecting consumers, the

[318] *Id.* (explaining that allegation intended to demonstrate AbbVie's conduct was cause-in-fact of monopoly prices).

[319] *Id.* at 844 (explaining that plaintiffs' use of word "could" signals "they do not intend to prove that prices were going to fall but-for the litigation").

[320] *Id.*

[321] *Id.* at 845 ("Nothing in the complaint demonstrates a basis to predict the requisite timing to establish plaintiffs' injury.").

[322] *Id.* at 844 (explaining that patent, not AbbVie's conduct, was but-for cause of monopoly prices).

[323] *See* Hacohen, *supra* note 35, at 528 (emphasizing difficulty of private litigants successfully alleging sham litigation claim); *see also* Amici Curiae Brief of 66 Professors, *supra* note 256, at 22 ("It is not consistent . . . to require a plaintiff demonstrating antitrust injury to prove precisely what would have happened in a but-for world that, by definition, has not occurred.").

[324] Amici Curiae Brief of 66 Professors, *supra* note 256, at 22 (arguing that requiring private plaintiffs to prove what would have happened is inconsistent with the Supreme Court's holding in *Actavis* that the "relevant anticompetitive harm" is "prevent[ion of] the risk of competition" (quoting FTC v. Actavis, Inc., 570 U.S. 136, 157 (2013))).

[325] *Actavis*, 570 U.S. at 157.

FTC has taken a particular interest in antitrust enforcement in the healthcare and pharmaceutical industries. Because the FTC need not demonstrate antitrust injury, the FTC could avoid this near-impossible causation issue, making it much easier to successfully demonstrate an antitrust violation. Further, the FTC has the remedial tools to correct the harm: the FTC has the ability to secure injunctions or cease and desist orders. The FTC could preclude assertion of these questionable patents and prevent these collusive settlement agreements, allowing the biosimilars to enter the market and drive down drug prices. Further, the FTC's potential disgorgement remedy could retrieve some of the monopoly profits the biologic manufacturers extract via their patent thickets. Even if the remedy is not regularly employed, the potential threat of being forced to disgorge profits would likely deter biologics manufacturers from creating patent thickets that could subject them to such scrutiny. Therefore, FTC enforcement of the antitrust theories discussed in this Section would increase the likelihood of success and serve as a sharp deterrent to future anticompetitive patent thicket misuse.

CONCLUSION

Biologic drugs present the cutting edge of pharmaceutical technology, fighting diseases previously considered untreatable and improving patient outcomes across medical disciplines. Developing these drugs is expensive, and the companies that bring these life-saving medicines to market deserve an exclusive period to recover their investment. However, this exclusivity period must be finite, and companies must not be allowed to exploit current law to unfairly preclude competition. Because of the complexity of biologics, the BPCIA regulatory scheme, and the quirks of patent law, biologics manufacturers are able to obtain vast patent thickets and assert them aggressively against biosimilar manufacturers, potentially resulting in anticompetitive settlements. Accordingly, antitrust principles should be able to strike back, attacking the formation of patent thickets, their aggressive assertion, and the use of anticompetitive settlements.

Biosimilar availability allows a greater population of patients to access these medicines at a lower cost, improving health outcomes in the United States. By creating patent thickets around their blockbuster drugs, biologic manufacturers unfairly appropriate these benefits, deriving additional market exclusivity and greater profits at the cost of patient health. With an antitrust remedy, the United States could decrease the barriers to biosimilar competition and return the benefits of a competitive market to the patients who rely on these medicines.