STRATEGIC PATENTING: EVIDENCE FROM THE BIOPHARMACEUTICAL INDUSTRY

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Despite much theoretical attention, empirical investigations causally exploring how the threat of entry leads incumbents to take certain strategic deterrent measures remain scarce. This is further true in the case of one measure thought to be strategically deployed in innovation-dependent industries: patents. We attempt to fill this gap while exploring strategic patenting practices by pharmaceutical manufacturers, particularly manufacturers of biological drugs, which now account for fifty percent of prescription-drug spending. Drawing on different sources of plausibly exogenous variation in the threat of entry by competing biosimilar competitors and building the first known database of patents linked to all FDA-approved biological drugs, we find robust evidence that biologics manufacturers are heavily turning to patents on secondary drug features to achieve exclusionary purposes that go beyond the traditional justifications of the patent system.

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I. Introduction

A substantial body of scholarship in industrial organization has addressed the strategic measures that incumbents take to block or deter entry by competitors. The strategic tools explored include such things as investments in capital capacity (Spence 1977; Fudenberg and Tirole (1983), long-term contracting (Aghion and Bolton 1987); advertising (Schmalensee 1983), and product differentiation (Schmalensee 1978). This paper will explore an additional strategy that either independently or in conjunction with these other strategies aims to forestall entry: patenting. Patents of course are meant to exclude entry to allow firms to recoup investments in research and development (Nordhaus 1969). However, firms may strategically use patents in ways to benefit from periods of exclusivity in excess of socially desirable levels (Frakes and Wasserman 2023).

Much of the scholarly attention directed towards strategic entry-blocking measures has been theoretical (Ellison and Ellison 2011). A key methodological challenge inhibiting the literature's attempts to empirically test for such behaviors has been the inability to find plausibly exogenous shocks to the threat of entry by competitors (Goolsbee and Syverson 2008; Righi and Simcoe 2023). In the patent context, a perhaps even more fundamental challenge has been data-related: the inability to link patents to specific products (Righi and Simcoe 2023). In this paper, to help address this important gap in the empirical literature on entry deterrence, we attempt to overcome these two challenges while testing for strategic patenting in an industry associated with nearly $800 billion spending in the U.S. annually: pharmaceuticals (Tichy et al. 2025).

The scope for strategic drug patenting is made possible by the fact that manufacturers may acquire multiple patents per drug. Beyond the primary molecule, they may patent "secondary" drug features, such as routes of administration, methods of use, devices, and manufacturing processes. Scholars have suggested that manufacturers may take advantage of this scope and "evergreen" by seeking secondary patents years after filing the primary molecule patent (Kesselheim and Avorn 2006; Hemphill and Sampat 2013), extending the period of time over which the drug faces patent protection (as each patent secures its own twenty-year term). Firms may also engage in patent "thicketing,"

building a dense web of patents for each drug to ensure that at least some survive legal challenges (Lemley and Shapiro 2005; Hall et al. 2021) and to compound litigation or licensing expenses for competitors.

Drawing from case studies demonstrating the number of patents associated with the blockbuster drug Humira and with several related drugs (Horrow et al. 2024), scholars have suggested that thicketing and evergreening practices are particularly pronounced in the case of "large-molecule" drugs, also known as "biologics," which are medications derived from living organisms. Despite the preliminary evidence set forth in these case studies, the full patenting landscape associated with biologics, along with the resulting implications for competition, remains unknown. This gap in the literature is meaningful given what we do know about observed levels of pricing for, and spending on, biologics. A given biologic can cost a patient between $10,000 and $30,000 per year, with costs exceeding $500,000 for the most expensive biologics (Chen et al. 2018). Though biological drugs represent only 2% of prescriptions written, spending on biologics represents close to 50% of net drug spending (Association for Accessible Medicines. 2019).

Why do we know so little about patents on biologics? The answer, in part, relates to the regulatory structure surrounding these markets.[1] With respect to small-molecule drugs—i.e., low-molecular weight medications that can be chemically synthesized—U.S. law has mandated since 1984 that brand-name manufacturers disclose their associated patents to the Food and Drug Administration (FDA). The FDA, in turn, publicly disseminates the resulting patent lists in something known as the Orange Book, a resource which has been heavily used by researchers.[2] The disclosure requirements for biological-drug patents, on the other hand, are very limited. We demonstrate that such requirements capture less than 4% of the true universe of biologics patents.

[1] The answer also relates to the difficulty and time associated with building a biologics patent database, along with the need for both scientific and legal expertise in its construction. One of us (Wasserman, J.D., Ph.D. Chemical Engineering) trained and supervised our post-doctoral researcher (Ph.D. Chemistry), who worked full-time over a nearly two-year period (beginning in September 2023) to build the relevant database.

[2] These data have been heavily used by researchers, including health and innovation economists, with the National Bureau of Economic Research housing archived versions of the Orange Book: https://www.nber.org/research/data/orange-book-patent-and-exclusivity-data-1985-2016, which were digitized by Heidi Williams and discussed further in Durvasula et al. (2022).

To fill this much needed gap, we build the first comprehensive patent database linked to all 515 FDA-approved therapeutic biologics. Our key inclusion criterion is to identify patents that would be infringed if a biosimilar—i.e., the large-molecule analog to generics—were to enter the market to compete with the relevant drug. We searched patent texts to identify possible patents associated with each FDA-approved biologic and then read each identified patent to assess it against the stated inclusion criteria and to code the relevant patent type (e.g., device patent). We structured the searches in multiple stages of different scopes to cast a wide enough net to identify all possible patents, but not so wide as to render the necessary coding and validation process unmanageable given the length and complexity of patent documents. After a nearly two-year full-time construction process, the resulting database consists of 11,595 drug-patent pairs.

Using these data, we begin our investigation into strategic patenting with a preliminary empirical exercise in which we establish the degree to which drug patenting is causally driven by an incumbent manufacturer's general fear of biosimilar entry. To draw on a plausibly exogenous shock to this entry threat, we take advantage of an opportunity afforded by Congress in 2010 when it created an abbreviated pathway for FDA approval of biosimilars. We find that this creation of the biosimilar marketplace led biologics firms to greatly accelerate the degree to which they sought patents on existing biologics, with no such acceleration in the case of existing small molecules.

To begin to illuminate thicketing and evergreening behaviors specifically, we then set forth certain descriptive statistics surrounding the patent portfolios that we uncover. Biologics are associated with substantially more patents per drug than small-molecule drugs: 22.7 versus 3.8, on average. Moreover, the extent to which subsequent patents prolong patent lives of drugs is substantially greater for biologics. For instance, the median number of years between the expiration date of a given biologic patent and that of the first-expiring patent associated with the relevant drug is 12 years, notably greater than the 2.7-year median for small-molecule drugs.

But are these statistics the product of "strategic" behavior as that term is used in the literature? That is, were the patents in question acquired to achieve exclusionary purposes

that go beyond the traditional, welfare-increasing rationale for patents—that is, beyond simply recouping the research and development expenses associated with the innovations underlying the specific patents (Blind et al. 2006, Moser 2013)? Or might this evidence of portfolio thickness and a large share of later-expiring patents merely be the product of a traditional development process over secondary drug features? The heart of our analysis will confront this fundamental question.

We take two approaches to assess whether patents on secondary biologics features are being acquired for purposes that go beyond simply fostering the innovations associated with such features. First, we investigate whether biologics manufacturers are acquiring patents on new features of a drug in a seeming attempt to block competition not just on the drug product with that new feature but on all versions—old and new—of the relevant drug. We theorize that firms hoping to use patents to achieve such spillovers will optimize the amount of time patents on some feature of the relevant drug will be in effect—i.e., they will deliberately, as opposed to incidentally, evergreen. They will do so by filing follow-on patents prior to but as close as possible to the expiration of the initial patents associated with the drug. Drawing on staggered timing of long-predetermined dates as to when certain drugs' initial, primary patents expire and estimating event-study specifications (Wing et al. 2024 and Cengiz et al. 2019) in windows around these expirations, we find striking evidence suggestive of such strategic timing.

In a second attempt to assess whether biological drug patenting departs from the traditional objective of simply justifying the new innovations, we assess whether manufacturers take advantage of inadequate screening at the U.S. Patent & Trademark Office (Patent Office) and acquire non-innovative secondary patents that further exclusionary goals. Using various markers of the novelty and nonobviousness of patent applications, we find evidence that some portion of those patents filed just before the initial patent's expiration are of questionable innovativeness.

Altogether, these findings suggest that biologics patent portfolios have the potential to meaningfully forestall entry by biosimilars. To begin to shed light on whether such practices block entry in practice, we set forth certain descriptive statistics surrounding the

biologics marketplace. These descriptive findings are consistent with a meaningful blocking effect, including the demonstration of a six-year longer period before competitive entry for biologics relative to small-molecule drugs—i.e., for drug types associated with greater thicketing and evergreening behaviors.

Among other robustness checks, we also explore each of the inquiries discussed above separately by patent type. Should our findings be reflective of strategic gamesmanship, one might expect to observe our strategic markers more frequently with respect to drug features that are more amenable to producing an associated patent application in a constrained time frame, for instance through subtle manipulations of existing technologies. We predict, and indeed find, that this is more likely the case for device, formulation, and manufacturing patents.

Congress has recently proposed various reforms aimed at curbing evergreening and patent thicketing practices. In a final exercise, we simulate the extent to which these proposals (subject to certain assumptions) will actually target these practices.

Our paper proceeds as follows. In Part II, we offer a literature review on strategic patenting and a brief background on the biologics regulatory process. In Part III, we discuss the construction of the novel biologics patent database. In Parts IV-V, we explore the strategic patenting behaviors of biologics manufacturers. In Part VI, we explore the association between these patenting practices and biosimilar entry. In Part VII, we explore the potential of certain policies aimed at reducing biologics patent thickets. In Part VIII, we conclude.

II. Background

A. Literature Review

In Part V below, we discuss certain aspects of the empirical literature exploring the deterrent measures employed strategically by incumbents. In this Part, we focus more specifically on those studies that have addressed patents as a particular strategic tool.

To begin, a number of studies have used Orange Book data to describe the patent portfolios of small-molecule drugs. For instance, Hemphill and Sampat (2011, 2013) fail to find evidence of substantial thicketing in the small-molecule marketplace, documenting

a mean of only 2.7-3.9 patents per drug across different samples. Hemphill and Sampat (2013) do find evidence suggestive of evergreening among small molecules, with secondary patenting extending nominal patent terms of drugs by roughly 3 years on average. However, they find that litigation challenges by generic manufacturers are effective at notably reining in such extensions.[3]

Outside of the pharmaceutical context, other studies have attempted to shed light on the existence of strategic patenting through indirect correlational exercises. That is, they estimate the relationship between various patent-based measures—e.g., patenting volume or patent valuation—and metrics indicative of innovative output. Negative or weak correlations are suggestive of uses of patents that deviate from their traditional justification. For instance, Abrams et al. (2019) documents an inverse-U-shaped relationship between forward patent citations and patent-linked revenue, with the downward-sloping portion of the curve reflecting strategic patents.[4] Hall and Ziedonis (2001) documents a growing disconnect between firm-specific patenting volumes and research and development expenses.[5]

Several aspects of these studies leave them to fall short of evidencing strategic behaviors. Negative relationships between revenues generated from patents and the technological advancements associated with them may reflect the strategic nature of such patents but may also reflect certain features of the underlying marketplace—e.g., a marketplace that does not necessarily price its products based on their scientific value, such as with pharmaceuticals (Hemel and Ouellette 2023). More broadly, citation-based approaches are limited by attempting to infer strategic motivations behind patenting based

[3] The closest the literature has come to showing comparable statistics for biologics is from a limited database developed by the Initiative for Medicines, Access & Knowledge (I-MAK), which has mapped the patents associated with the six highest revenue-generating biologics, though not following the biosimilar-infringement inclusion criteria that we set forth in Part III, leaving their analysis overinclusive. Using these data, Horrow et al. (2024) find that these six biologics are associated with an average of 8 patents when approved by the FDA but an average of 41 patents 13 years after approval. They acknowledge their results may not generalize to the over five hundred other large-molecule drugs that have been approved to date, which we study for the first time in this paper. Beyond this generalizability question, the largely descriptive analysis that the I-MAK studies set forth fails to fully probe the consequences of, and the strategic nature of, such practices, which we aim to do in Parts V and VI.

[4] A number of related studies have likewise explored the relationship between the private value of patents and the scientific / technological value of patents (as usually proxied by forward citations), including Kogan et al. (2017), Kelly et al. (2021), and Veihl (2022).

[5] Other studies have surveyed research and development departments at firms, where respondents have indicated exclusionary uses patents for reasons unrelated to justifying their innovations—e.g., building thickets to enhance cross-licensing negotiations (Cohen et al. 2000).

on the effects of patents granted rather than based on an empirical evaluation of the firm's choice to patent in the first place, leaving room for confounding explanations. The R&D-based studies, moreover, cannot rule out that their findings of a weakening connection between R&D spending and patenting can be explained by the efficiency of R&D spending improving over time (Kortum and Lerner 1999).

In our study, we take a more direct approach in testing for strategic patenting. We explore firm decisions within specific, identified product spaces regarding if and when to patent in order to achieve a particular objective. Moreover, we do so while employing certain causal-inference tools to test whether these strategic patenting decisions are caused by the competitive conditions of the specific product space.[6]

Our study is also related to a range of other literatures. These include studies (i) exploring how drug-manufacturer behavior changes in the shadow of patent expiration (Ellison and Ellison 2011; Scott Morton 2010), (ii) generally exploring the impacts of firm patenting on marketplace outcomes—e.g., cumulative innovation (Sampat and Williams 2019; Galasso and Schankerman 2015; Hegde, Herkenhoff, and Zhu 2023), and (iii) broadly exploring the connection between innovation and competition in the pharmaceutical industry.[7]

B. Background: Drug Types and Pharmaceutical Regulatory Approval Process

Biologics have complex molecular structures often consisting of proteins, antibodies, or cell-based therapies. Because they are usually derived from living organisms/cells, they are difficult to reverse engineer and impossible to replicate exactly. This stands in contrast with "small-molecule" drugs, which are less costly to produce and which possess simple molecular structures that can be easily reverse engineered. These differences are more than just scientific; they also garner separate regulatory treatments.

[6] Our methodological approach is close in spirit to that taken by Righi and Simcoe (2023), which also links patents to specific product spaces—in their case, specific technology standards—and likewise explores how patenting practices change in response to a shock in the relevant competitive environment. Specifically, they find evidence that firms opportunistically file continuation patents to modify the claims of parent applications that were filed before the relevant standard is published, where these claim modifications ensure that the claims cover the newly published standard.

[7] See Cunningham et al. (2021) for a recent literature review.

The Hatch-Waxman Act (HWA) of 1984 created an abbreviated pathway for generics to enter the small-molecule market. To receive FDA approval, generics need not replicate the clinical trials of brand-name drugs (demonstrating safety and efficacy), but, instead, need only demonstrate that their product is bioequivalent to the already FDA-approved small-molecule drug. The HWA further requires the brand-name manufacturer to provide the FDA with a list of patents that would be infringed if a generic is launched before the expiration of these patents, information which is ultimately included in an FDA publication commonly known as the Orange Book. The FDA can approve the generic after all of the Orange Book-listed patents expire or after a thirty-month stay during which the generic and brand engage in specialized patent-dispute procedures.

The HWA did not address the approval and patenting of biologics. It was not until 2010, with the passage of the Biologics Price Competition and Innovation Act (BPCIA), that the FDA was empowered to develop an abbreviated pathway to approve biosimilars. Similar to the HWA, the goal of this pathway is to obviate the need for biosimilars to demonstrate safety and efficacy through their own clinical trials. However, certain critical differences exist between the HWA and its biologics counterpart, the BPCIA.

First, given the inherent replication challenges associated with biologics, biosimilars seeking approval must demonstrate that there are no clinically meaningful differences between the biosimilar and the original FDA-approved biologic. This demonstration of "biosimilarity" is a more drawn-out and expensive process than that required to show bioequivalence in the small-molecule context (Atteberry et al. 2019). Second, in contrast to the HWA, the BPCIA neither links FDA approval of biosimilars to the patent rights associated with biologics nor does it mandate that biologic companies provide patent information to the FDA upon the filing of a license application.

Between the BPCIA and follow-on legislation passed in 2020, federal law does create certain patent-disclosure mechanisms for brand-name biologics, culminating with the FDA dissemination of something known as the Purple Book.[8] However, for reasons

[8] Throughout, we will refer to the original biologics drug as the "brand-name" and its associated producer as the "brand-name manufacturer." We use this terminology to facilitate comparisons between small- and large-molecule marketplaces. Technically, in the context of biologics receiving FDA approval, the original biologic goes by the term "reference product" and its associated manufacturer goes by the term "reference sponsor."

that we set forth in the Online Appendix, the comprehensiveness of the Purple Book falls far short of that of the Orange Book, the key difference being that disclosure is not mandatory for large molecules. With only 424 current entries in the Purple Book, it captures less than 4% of the biologics patent database that we construct, a construction exercise to which we now turn.

III. Construction of Biologics Patent Database

One of the key implications of the regulatory structure set forth in Part II is that, while scholars have been able to take advantage of the Orange Book to study the small-molecule drug-patent landscape, they have been unable to benefit from a corresponding resource in the biologics context. To address this gap, we build a database of patents associated with 515 biologics licensed and approved by the FDA. Given that innovation incentives and markets differ considerably between preventives and treatments (Kremer and Snyder 2015), as do the way in which they are regulated, we focus our analysis on therapeutic biological drugs rather than vaccines.

Before discussing the search steps that we take to construct the biologics patent database, we first address the theoretical foundations underlying its scope.

A. Inclusion Criterion

The key inclusion criterion that we use to guide our selection of patents is as follows: we identify patents that would possibly be infringed if a biosimilar were launched to compete with the relevant drug. Doing so, and consistent with the aims of our analysis, we capture situations in which the included patent may have a meaningful competitive blocking effect in the relevant market. We do not wish to be overinclusive in this regard to avoid overstating the degree of market interference that biologics patent portfolios actually impose. To be sure, not all patents acquired by brand-name firms meet the above inclusion condition. A frequent context in which this criterion fails is when a brand-name firm acquires a patent on a new drug indication but where the FDA has not approved that

indication.[9] To see this more clearly, let us consider several abstract scenarios, beginning with one where the criterion is, in fact, met.

Scenario 1. Consider a biologic, Drug X, that is FDA approved to treat rheumatoid arthritis and that is marketed by Firm A. Moreover, consider a patent held by Firm A that claims rheumatoid arthritis as a method of use for Drug X. Assume Firm B seeks approval of Biosimilar Y to treat rheumatoid arthritis and demonstrates its biosimilarity to Drug X to the FDA. Though Biosimilar Y may receive approval to enter the market and compete with Drug X, such entry may be blocked by Firm A's assertion of its patent against Firm B. This patent has a meaningful biosimilar-blocking effect and will thus be included in our sample.

Scenario 2. Building on Scenario 1, now assume Firm A receives a patent claiming use of a novel dosage of Drug X to treat Crohn's disease. Further assume the FDA has not authorized Drug X at this new dosage to treat Crohn's. It is illogical to think of biosimilar entry for this drug/dosage combination to treat Crohn's, as there is no corresponding originator/reference biologic previously approved to treat Crohn's. In other words, the inclusion criterion fails in this scenario because there is no possible biosimilar that has relevance to this patent. Accordingly, this patent would not be included in our data.

Scenario 3. Continuing from Scenario 2, while no biosimilar can be approved to treat Crohn's, another firm may proceed through *full* clinical trials to get approval for the relevant drug/dosage combination for Crohn's. Assume Firm C does so. In this event, the patent from Scenario 2 does have relevance as Firm A could sue Firm C for infringement. However, in this instance, we would no longer be discussing Firm A's patent blocking *biosimilar* entry, in which case this patent still fails the inclusion criterion. Rather, Firm C in this latter example would be considered an originator of a *new biologic*, not a biosimilar.

Discussion. Of course, Scenario 3 only raises the question as to why we do not broaden our inclusion criterion to capture patents that not only block biosimilar entry but also block entry of new biologics. We elect not to extend matters this far as Firm A's patent—and the associated threat of an infringement suit—is likely not directly

[9] For similar reasons, another context in which the criterion fails is when the FDA had only approved the biologic drug alone but firms receive combination patents that claimed an FDA-approved biologic to be used in combination with another chemical compound.

discouraging Firm C's entry in Scenario 3. What is likely to block Firm C from entering is instead the considerable expenses needed to conduct the relevant clinical trials showing safety and efficacy of using the relevant drug to treat Crohn's. Among other reasons, Firm C may be unlikely to undertake these expenses given the possibility that it winds up splitting the Crohn's market with other producers if some physicians elect to prescribe Drug X off-label for treating Crohn's.

Our decision to only include patents that would be infringed by a biosimilar if they were to enter the market tracks that taken by Congress in calling for the construction of the Orange Book in the small-molecule context.

B. Search Process

In the Online Appendix, we set forth the various steps taken to identify patents meeting this criterion. The most significant step entails conducting patent searches utilizing Orbit Intelligence patent analytic and search software. A key challenge in implementing this search is that patent documents do not contain text fields that directly speak to our inclusion criterion. For instance, imagine that a search over Humira's chemical name "adalimumab" flags a patent with "adalimumab" in its claims text. It would be inaccurate to include that patent as a Humira patent if a careful read reveals that the claims speak to using adalimumab in ways not authorized by the FDA. Relatedly, it would be inaccurate to include the patent in our database if a careful read reveals that adalimumab was not actually the functional subject of the claims.

To avoid the risk of otherwise misapplying our inclusion criteria through an attempt to automate detection of these kinds of failures, we read and hand-code all patents before including them in our database. Nonetheless, we design a search protocol to manage the scope of this validation exercise, attempting to cast a net that is wide enough to capture all likely patents, but not too wide so as to sacrifice tractability.

To fine-tune this targeting process, we operationalize this protocol in different stages, across which we trade off on different search parameters. In a first stage, we start

with a narrow framing of one parameter—mainly, limiting the search to corporate entities[10] associated with developing the relevant biologic—while searching broadly across other search parameters—e.g., searching the patent claims of all patents held by those entities for the inclusion of the drug class, Trade name, chemical name or chemical identifier code of the relevant biologic.[11] In the next stage, we take a broader framing on that first parameter—no longer limiting the assignee of the patent —but a narrower framing on the other parameters—e.g., searching only the claims of patents with the same Trade name, chemical name, or chemical identifier code. Third, we search for patents that contain the biosequence of the relevant biologic. Finally, we code each included patent for its type—e.g., device, formulation, etc.

Our primary results include pending patent applications in the associated patent portfolios.[12] We do so given that biologic patenting activity has particularly accelerated in recent years and the vast majority (over 75%) of these applications will ultimately issue, in which case their inclusion is consistent with our goals of depicting the degree to which biologics patenting activity may forestall competitors moving forward. Moreover, we note that our goal is not necessarily to provide a snapshot of biologics patent portfolios at the present but rather to provide a sense of the blocking effects of portfolios when they were active. As such, we include patents that have expired to provide a sense of the portfolios associated with older biological drugs.

The resulting dataset consists of 11,595 drug/patent pairs across the 515 therapeutic biologics approved by the FDA to date. Six of these biologics do not have any patents (issued or pending) in their portfolios. Roughly 73% of biologics patents are unique to a single drug product, whereas 27% of biologics patents are associated with more than one drug—e.g., the same patented manufacturing process is associated with more than one approved biologic.

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[10] Specifically, we limit the search to corporate entities and any subsidiaries thereof who filed for FDA approval and/or were involved in the development, manufacture, or marketing of the biologic, as we discuss in greater detail in the Online Appendix.
[11] This first stage is slightly different with respect to a search for device patents as we discuss in the Online Appendix.
[12] Nonetheless, we exclude applications that have been formally abandoned with the Patent Office, as they will ostensibly never issue and have blocking effect.

Figure A1 of the Online Appendix breaks down the drug/patent pairs into patent type. Main/primary compound patents comprise 13% of the sample. The remainder represent different types of secondary drug patents, including device patents (16%), manufacturing process patents (25%), formulation patents (19%), and method of treatment patents (27%).[13]

C. Brand Level

Each secondary patent that a biologics manufacturer obtains does not necessarily have immediate blocking power over all biosimilar competitors to the relevant drug. For instance, consider a patent on a new formulation of a biologic, Drug K, allowing it to be administered via injection as opposed to infusion. A competing biosimilar to Drug K that attempts to enter the market under the original infusion product would not necessarily find itself infringing on the injection patent. Given that our goal is to explore how patents block competitive entry, should we then treat Drug K as two separate observations—Drug K with infusion and Drug K with injection—and evaluate patenting within these separate drug products? We elect not to separate in this manner and instead organize our analysis at the drug brand level—i.e., Drug K collectively (Durvasula et al. 2023). The key reason behind this choice is that the blocking potential of secondary patents may spillover to impact entry by biosimilars that market a product lacking the relevant secondary drug feature.

To see this, continue with the above example. By introducing Drug K in injectable form—aided by its relevant patent—the manufacturer may shift the market for the molecule away from an infusion basis altogether, discouraging competitors from offering the older infusion version. Manufacturers may aid this shift through a number of business tactics, including campaigns aimed at inducing physician buy-in to the reformulation. "Product hopping" strategies of this nature have been the subject of much scholarship, regulatory action, proposed federal legislation, and litigation.[14] By keeping our analysis of

[13] In the Online Appendix, we provide more specific definitions of these different types. We note that given drugs often have multiple "main-compound" patents. This is because our definition of compound patents includes a patent that claims a biological compound, a specific conjugate, or a specific post-translational modification to a protein or antibody, which is a modification that occurs after the protein or antibody has been synthesized. Biologics often have multiple of these sub-types.

[14] For example, see Carrier and Shadowen (2016), Federal Trade Commission (2022), and Lemus and Ozkul (2023).

patenting behavior at the brand level, we make sure to include such hopping/shifting strategies among the scope of our strategic-patenting analysis, as we discuss in Part V.

IV. Preliminary Strategic-Patenting Analysis

A. Rationality Check: Effect of Competitive Threat on Patenting Frequency

To prime our ultimate investigation into the strategic patenting behavior of biologics manufacturers, we establish the degree to which biologics patenting is driven by a general desire to block competitive entry in the first place.[15] For these purposes, we test whether biologics manufacturers' amassing of patents was caused by the very initiation of the biosimilar competitive threat. To capture this initiation, we take advantage of an unusual research opportunity afforded by Congress in March, 2010 when it passed the BPCIA (discussed above). Again, the BPCIA authorized an abbreviated pathway for biosimilar approval, allowing biosimilar firms to rely on the clinical trials associated with the originator biologic. This development obviated the need to go through the considerable expense of demonstrating to the FDA the safety and efficacy of the relevant drug, an expense biosimilar firms are thought to be otherwise unwilling to occur.

Though an important and under-studied question, our aim with this exercise is not to understand how the BPCIA impacted development of new biologics altogether. Rather, we aim to explore how the BPCIA incentivized firms to engage in strategic patenting in order to stem off the new biosimilar threat. Accordingly, we explore the patenting response to the BPCIA associated with those biologics that were already approved—and thus ostensibly already existed—prior the BPCIA. Did this threat of new competitors to the existing drugs induce firms to build patent portfolios to protect their market shares surrounding such existing drugs?

In Panel A of Figure 1, we show how biologics patenting levels (for those drugs in existence by 2009) evolves year-by-year leading up to and following the BPCIA. Specifically, we focus on the year in which the relevant patent was filed and estimate the

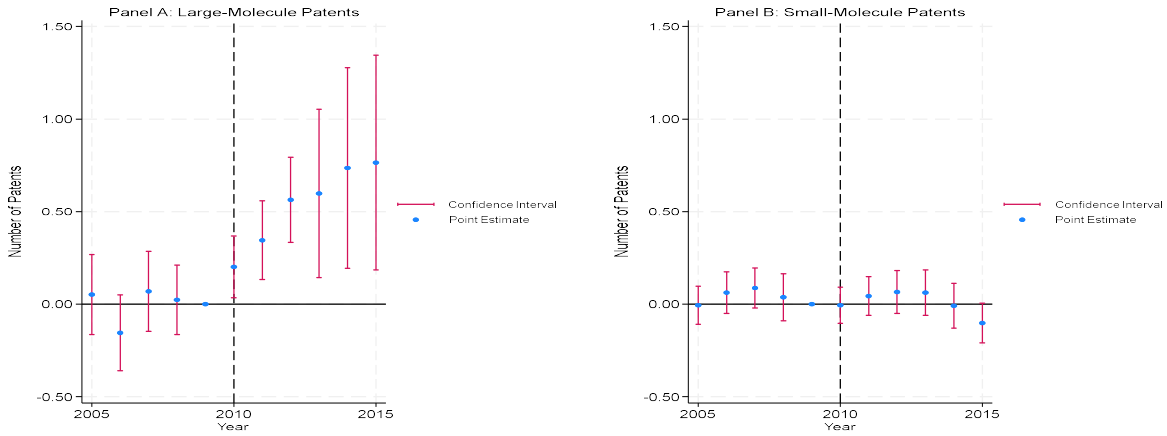
[15] At first blush, this might seem obvious; however, we note that the literature has discussed motivations to patent beyond simply desires to exclude competitors, including information-based and signaling motivations (Farre-Mensa et al. 2019, Harhoff 2009, Czarnitzki et al. 2007, Long 2002) and desires to improve bargaining positions in attempts to secure licenses (Carrier and Tu 2024).

following specification over the 2005-2015 period, where the unit of observation is a given drug-by-year cell:

(1)
$$Patent_Count_{it} = \alpha + \delta_i + \sum_{t=2005}^{2015} \beta_t YEAR_t + \varepsilon_{it}$$

where i denotes the individual drug and t the calendar year of filing and where δ_i captures drug fixed effects. Patent_Count$_{it}$ captures the number of patents associated with drug i in our database with an initial filing date of year t.[16] We then plot the estimated β_t coefficients.

Figure 1. Patenting Activity in Years Leading up to and Following BPCIA, Separately for Large- and Small-Molecule Drugs and Limited to Drugs that Were FDA Approved By 2009



Notes: Panel A reflects estimation of specification (1) among large-molecule drugs approved by 2009. Panel B reflects estimation of specification (1) among small-molecule drugs approved by 2009. N = 1,441 drug-year cells in Panel A. N=3,025 drug-year cells in Panel B. 95% confidence bounds are indicated by vertical bars.

As demonstrated by Panel A, biologics patenting counts among those drugs approved by the time of the BPCIA fluctuate a little year-by-year prior to the BPCIA's

[16] To provide a sense as to how both the annual trends in patenting differ between large and small molecules and how the absolute magnitudes of such annual changes compare, we estimate Ordinary Least Squares specifications to produce Figure 1. In Figure A2 of the Online Appendix, we show a corresponding figure that draws from Poisson specifications. Interpretation issues aside, the pattern in the figures is virtually identical between the OLS and Poisson approaches. We also limit the analysis to drugs that began patenting by the beginning of the observation window (2005), though our analysis is virtually unchanged if we make no such restriction.

adoption but generally remain flat. In the year in which the BPCIA is passed and thereafter, biologics patenting volume begins to increase notably. By 2012, the annual patenting volume has doubled the 2009 level.

Consistent with a causal effect, this sharp acceleration in annual patenting following 2010 is unique to biologics, as we observe no such increase in small-molecule patenting as demonstrated by Panel B, where we estimate a similar specification on small-molecule drugs likewise approved prior to 2010. In Figure A3 of the Online Appendix, we estimate a corresponding difference-in-differences specification and confirm the statistical significance of the larger biologics response.

B. Descriptive Analysis of Patent Thicketing and Evergreening Behaviors

1. Patent Thicketing

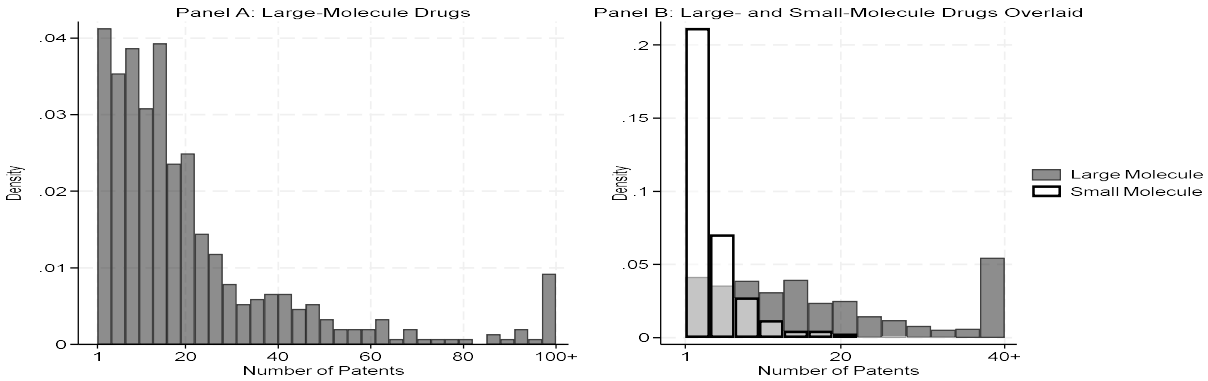
Having just established that patenting volume appears to be heavily associated with the threat of biosimilar competition, we now turn to quantifying just how thick given biologics patent portfolios are. In Panel A of Figure 2, we show the distribution of per-drug patent counts across all FDA-approved biologics. To offer a frame of reference, we show in Panel B the large-molecule distribution overlaid with the corresponding distribution of per-drug patent counts across all small-molecule drugs represented in the FDA's Orange Book.[17] As is readily evident from Panel B, large-molecule drugs tend to have substantially more patents than small-molecule drugs. Virtually no small-molecule drugs have portfolios larger than 20 patents, whereas roughly 35% of biologics patent portfolios exceed that amount (with meaningful mass in biologics portfolios even past 100 patents per drug). The average patent-per-drug of biologics is 22.7, in comparison with 3.8 for small-molecules.[18] Altogether, the number of patents that biosimilars need to navigate

[17] For the Orange Book data, we use the small-molecule dataset compiled in Frakes and Wasserman (2023) and update it to reflect the most recent Orange Book data from the FDA. These data amount to a series of snapshots of the Orange Book over time to ensure that we collect information from patents that were ever listed in the Orange Book (even if delisted at some point).

[18] We acknowledge there is a comparability challenge inherent in Figure 2 in that Congress did not require the listing of manufacturing patents in the Orange Book. Unfortunately, we are not aware of a comprehensive database in the small-molecule context that was constructed through a search process similar to that taken in this paper (though, we are presently building such a database). Nonetheless, we do not believe the omission of small-molecule manufacturing patents from the FDA's Orange Book impacts the effective comparison we are attempting to make in Figure 2. After all, manufacturing processes are simply less critical in small-molecule contexts in the first place. For further validation, we turn to the I-MAK database, which provides patent information on the top four selling small-molecule drugs, including those listed and not listed in the Orange Book. There are 59 Orange Book patents collectively across these four drugs, and I-MAK finds that these drugs are associated with 16 method of production / process patents. Accordingly, the small-molecule

before entering the large-molecule market greatly exceeds that of small-molecule generics.[19]

Figure 2. Histogram of Number of Patents Per Drug Across FDA-Approved Biologics, with and without Overlay of Small-Molecule (Orange Book) Patents-Per-Drug Histogram



Notes: Panel A is from our hand-collected and coded data on biologics patents across all 509 large-molecule drugs with at least one patent (excluding 6 drugs with no patents). Panel B overlays the distribution from Panel A with the corresponding small-molecule distribution, using data from Frakes and Wasserman (2023) on 2,032 small-molecule drugs represented in the FDA's Orange Book. In each case, each observation represents a given trade-name as registered with the FDA.

2. Evergreening

Of significance is also the degree to which patents in these dense portfolios extend the period of time over which a patent actively protects at least some aspect of the relevant drug.[20] A straightforward way to preliminarily summarize these extensions for a given patent is to calculate the difference in years between the focal patent's expiration and the expiration of the first-expiring patent associated with the relevant drug. Beginning with biologics, we show a histogram of this extension measure in Panel A of Figure 3, organizing the data at the patent-drug pair level. In Panel B, we overlay this large-molecule histogram with its small-molecule counterpart.

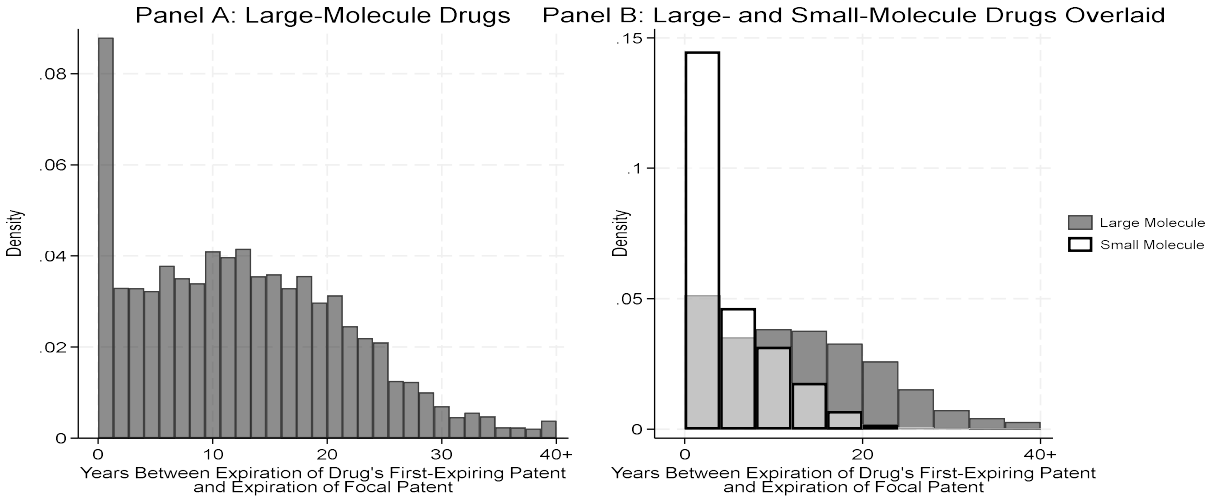
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patents missing from the Orange Book cannot likely account for the over five-fold difference in mean patents depicted in Figure 2 between small- and large-molecule drugs. Moreover, considering our aim in this paper of assessing the degree to which drug patents may block competitive entry, we note that the Orange Book patents identified in the I-MAK data were nearly eight times more likely to be asserted in litigation than the non-Orange Book patents.

[19] In Figure A5 of the Online Appendix, we show counterparts to Panel A of Figure 2 that separately depict the distribution of patent counts across biologics by different patent types.

[20] All expiration dates in this paper reflect patent term adjustments/extensions granted to the focal patent.

Figure 3: Histogram of Difference in Expiration Years Between a Given Patent and the Relevant Drug's First-Expiring Patent, Among Sample of Drug-Patent Pairs



Note: data in Panel A are from a sample of 11,595 biologic patent-drug pairs. Data in Panel B are from a sample of 7.772 small-molecule drug-patent pairs.

We document evidence of both a high level and high spread in the degree to which biologics patents extend the duration over which patents protect the relevant drug, in addition to evidence of notably stronger extensions for large relative to small molecules. We find that the average number of years between a patent's expiration and the relevant biologic's first patent expiration is 12.7 years, with a standard deviation of 8.2 years and a median of 12.0. The corresponding small-molecule numbers are as follows: mean of 4.7, standard deviation of 5.5 and median of 2.7 years.

V. Markers of Strategic Behavior

In this Part, we diagnose whether the descriptive statistics set forth in Figures 2 and Figure 3 are reflective of strategic practices. By strategic, we again mean exclusionary uses of patents that go beyond simply recouping the research and development expenses associated with the novel innovation underlying the relevant patent. We approach this

inquiry in two steps: (i) probing manufacturers' motivations by exploring the manner in which they time secondary patenting and (ii) exploring whether manufacturers are also receiving patents on non-innovative features.

A. Spillover-Motivations: Strategic Timing Analysis

1. Strategic Timing Analysis: Overview of Approach

We begin this strategic patenting inquiry with a competing-models exercise (Card et al. 2011). As we will discuss in sub-Part A(2), the key point of separation between the competing models will respect timing, mainly the year-by-year progression in the frequency of secondary patenting. To preview, we (i) predict what a temporal patenting path might look like for a firm that uses patents in the traditional way to recoup research and development expenses for new innovations, (ii) predict what that temporal path might look like for a firm that follows a particular strategic deviation from this traditional route—i.e., a maximizing-evergreening strategy, and (iii) assess whether firms' observed temporal patenting paths are more consistent with (i) or (ii).

We note that, consistent with those papers that have empirically explored how incumbents make strategic investments to block or deter entry, we do not test for strategic behaviors through the estimation of structural parameters (Dafny 2005; Ellison and Ellison 2011; Seamans 2012). The reduced-form approach that we do take with this competing-model exercise—which tracks within-drug changes in patenting activity over time and draws on staggered timing of pre-determined primary-patent-expirations—departs from the largely cross-sectional approaches taken by this literature to date and thus attempts to come closer to causal identification of the threat of entry on firm behavior. Our approach is closest in spirit to the event-study analysis of Goolsbee and Syverson (2008), though we estimate a stacked event-study specification rather than a two-way fixed effects specification to avoid the well-documented potential biases with the latter approach (Goodman-Bacon 2019). Let us elaborate on the specifics of this exercise.

2. Strategic Timing Analysis: Competing-Model Predictions

Traditional Patenting Model. First imagine a model in which a biologics manufacturer continuously engages in efforts to innovate over secondary drug features of an existing biologic and, when such innovations arise, markets new versions of the drug with the novel features. Assume the manufacturer approaches these secondary R&D activities with an intensity, *RD*, that evolves smoothly over time—that is, *RD(t)* is continuous and differentiable.[21] This may capture a development process with some amount of either growth or decay (or both). Further assume that each unit of *RD* produces a secondary innovation with probability *p*. In this case, the manufacturer would be expected to produce *pRD(t)* secondary-drug-feature innovations at time *t*, a function which will also be continuous and differentiable over time.

Finally, we assume that firms will file patents at time *t* to protect the innovations produced at time *t*, *pRD(t)*. This assumption is reasonable considering that the U.S. resolves patent races with reference to those who file patent applications first and considering that delaying the patenting of new innovations risks other patents or scientific publications emerging in the interim that would invalidate attempts to patent the innovation later. Thus, there will be a one-to-one mapping between *pRD(t)* and the temporal path of patenting. These patents will allow the manufacturer to market new versions of the drugs with the innovative features while excluding others from doing so. All told, under this traditional-patenting model, biologics firms will patent secondary drug features in the post-primary-patent-filing period in a manner that evolves smoothly over time.

To be clear, the findings of Figures 2 and 3 may be consistent with this model, since it does entail secondary patenting activity (i.e., adds thickness to drug patent portfolios) and since some of this activity will transpire in the years following the discovery of the primary compound.

Strategic-Timing Model. Now, imagine an alternative strategic-patenting model, where the manufacturers' motivation to patent a secondary feature extends beyond merely

[21] The purpose of this competing-models exercise would still be met if we relaxed this smoothness assumption in this traditional-patenting model and allowed for discontinuous jumps in development activity to occur at any point in time. In that case, the key feature of this traditional model that separates it from the strategic-timing model discussed below is that that one would not necessarily expect in the traditional model for those discontinuities to occur at the moment when the drug's initial patents expire (unlike in the strategic timing model).

facilitating the creation of a version of the drug with the new feature and blocking competitors from marketing drugs with that feature. In particular, envision a manufacturer aiming to use secondary patents on the new drug features as part of a broader scheme to exclude competition over all drug products associated with the given compound, including versions of the drug with the initial drug features.

To see this, recall the product-hopping strategy discussed in Part III. At the outset, we note that we do not formally model the entirety of this strategy as its basic theoretical structure has been much discussed in the literature to date.[22] We simply lay out the basic intuition, which produces straightforward testable predictions. The essence of this strategy is that, while creating a market for the new version of the drug, the manufacturer may also engage in an advertising campaign to induce providers to embrace the new version of the drug in lieu of older versions. Even if the initial patents on the drug have expired, and thus even if biosimilars can enter to compete against the initial version of the drug, the biosimilar manufacturers may be deterred from doing so knowing that the brand-name biologics manufacturer's advertising activities have helped shift the market to the new version, against which the new patents prevent the biosimilar from competing.[23]

To achieve this deterrence, the brand-name biologics manufacturer will aim to develop and patent the secondary feature prior to the biosimilar's ability to enter the market under the initial version—that is, prior to the expiration of the initial patents. If the manufacturer waits until after biosimilar entry on the first version, it runs the risk of physicians not being willing to adopt the new version after having already adopted the biosimilar for the initial drug product, a realistic risk in light of evidence over physician persistence in drug choice (Crawford and Shum 2005). Similarly, it may advantage the manufacturer to execute the product-shift prior to the initial patent expiration as physicians

[22] For a comprehensive discussion of product-hopping strategies by pharmaceutical manufacturers, see Carrier and Shadowen (2016). See also Huskamp et al. (2008), Feldman and Frondorf (2016), and Lemus and Ozkul (2023) for theoretical and/or empirical treatments of product hopping and for a review of the relevant literature.

[23] Considering classic models of product differentiation (Schmalensee 1978), the biosimilar may still be deterred even if this provider-inducement strategy is only partially successful and even if the sales associated with the compound itself are split among the different versions of the drug (Bokhari and Yan 2020).

may be less likely to adopt biosimilar versions of the initial drug product after having already shifted to the new drug product (Lemus and Ozkul 2023).[24]

If successful, this strategy may allow the initial manufacturer to maintain a monopoly over the compound itself—that is, blocking competition over the initial version and then the new version of the biologic. With this in mind, to maximize the rents associated with this strategy, the manufacturer will want to maintain this monopoly for as long as possible, which entails delaying on producing the new version of the drug until the end of the monopoly period over the initial version of the drug. In effect, this amounts to a deliberate attempt to evergreen and, for that matter, to maximize the degree of evergreening, as distinct from the traditional-patenting model, where patent-life extensions from secondary patenting were incidental to a normal development process.

Ultimately, there are two key features of this strategic model that separate it from the traditional model and that facilitate testing within this competing-models framework. First, the manufacturer's research and development over secondary drug features, *RD(t)* will be higher in the years prior to the year, *E*, in which the initial patent associated with the drug expires—i.e., the initial primary patent covering the relevant biologic's main molecule. *RD(t)* will then drop off after year *E*. Second, in this pre-expiration period, *RD(t)* will be highest in the period just before year *E*. Given that this development only produces innovation with probability *p*, as above, and given the need for time at the Patent Office to review the associated patent, which comes with temporal uncertainty, *RD(t)* is not likely to be fully concentrated at the very last moment before *E*, but will be ramping up in the years leading up to that moment. Taking this all together, this suggests that *RD(t)* will follow a temporal path of the following nature:

[24] A question arises as to what "initial patent" will serve as the reference point for this strategy. We model manufacturers as timing this deterrence strategy around the expiration of the drug's primary patent—that is, the main patent associated with the underlying compound (which we identify as the earliest "Main Compound" patent in our database for each drug). We acknowledge that, at the moment the drug's primary patent expires, it may not necessarily be the last expiring patent associated with the relevant drug's original product. Consider, for instance, a patent, Patent B, that is filed several years after the initial primary patent. Patent B would then expire several years after the primary patent. However, considering evidence that primary patents are more likely to survive legal scrutiny (Kyle 2016), the primary patent may remain the last expiring patent covering the initial drug product with confident legal validity. In this case, the primary patent's expiration remains particularly salient, and firms may wish to target much of their evergreening timing around this expiration date. If firms wait longer—e.g., for the expiration of Patent B—they run the risk of Patent B being invalidated in the courts and a consequent gap in patent coverage for the relevant drug.

$$RD(t) = \begin{cases} M(t), where\ M'(t) > 0, & t < E \\ M(t) - \alpha, & t \geq E \end{cases}$$

As with the traditional model, we assume the temporal patenting path will likewise follow the temporal structure followed by *RD(t)*. In other words, while the traditional model will evidence smoothness in patenting over time, the strategic model will (i) demonstrate a discontinuous dip downwards in patenting activity at the moment of the drug's primary-patent expiration and (ii) demonstrate an increase in patenting in the year's leading up to the primary-patent expiration.

The two points of separation between the competing models provide a straightforward means of testing for the presence of strategic patenting behavior and motivate our empirical analysis below. Specifically, our analysis will observe firms' secondary patenting activity in event windows surrounding the expirations of the relevant biologics' primary patents, where we will then test whether firms' secondary patenting activities drops upon the expirations of the biologics' primary patents and increase leading up to those primary expirations.[25]

3. Strategic Timing Analysis: Methodology and Results

Before explaining the specifications underlying this event-study approach, we first describe certain sample-construction choices. First, as above, to the extent firms bunch patenting practices prior to the expiration of the primary patent, some lead time is necessary to give the Patent Office an opportunity to review. Accordingly, in testing for such bunching, we center our event-window around the year prior to the primary patent's expiration and track patent-filing activity in the four years leading up to and following that centered year (for a 9-year window in total). Given the necessary review time, we acknowledge firms may still try to get their filings in sooner than one-year pre-expiration, but we nonetheless center our windows around the one-year-pre period as that year is effectively the last possible time to submit as part of this strategy.

[25] Our analysis here generalizes and builds upon the analysis set forth by Carrier and Tu (2024), which documented an uptick in patenting near the end of the term of Humira's primary patent. To be clear, our analysis will not directly test for evidence of all aspects of product shifting/hopping, as the focus of this paper is on strategic patenting practices, but we will nonetheless test the key role played by patents in this broader deterrence strategy (Carrier and Shadowen 2016).

Second, in tracking patenting activity over this event window, we focus on the filing of non-continuation patents, as continuation patents keep the expiration date of their earlier parent application and thus do not directly add to the effective lives of patents.[26] Third, we focus on event windows in the post-2010 period. As discussed in Part IV, Congress created the biosimilar threat at this time, leaving strategic evergreening motivations less relevant prior to this time.[27]

These sample restrictions leave us evaluating 80 biologics experiencing a primary-patent expiration in the event window—i.e., "treatment" biologics. We estimate event-time trends after first stacking the event-windows for each such treatment biologic on top of one another. We take two approaches to account for possible confounding of event and calendar time. First, we take advantage of the fact that calendar and event time do not perfectly overlap given staggering of primary-patent expirations and estimate a simple stacked event study design over the treatment drugs. Second, we take a more comprehensive approach that draws inspiration from the stacked event-study difference-in-difference literature (Wing et al. 2024; Cengiz et al. 2019; Desphande and Li 2019) and include control drugs within each layer of the stack to account further for calendar-time trends, which we discuss below. In each approach, our unit of observation is a drug-by-event-year period—where event time is measured with reference to the timing of patent filings relative to primary-patent expiration. Our key dependent variable is the number of patents recorded in our database for that drug-by-time cell. Our primary analysis estimates Poisson specifications.[28] We begin with the simple event-study specification without control drugs:

$$Patent_Count_{ie} = \exp\left(\alpha + \delta_i + \sum_{e=-4}^{4} \beta_e EXPIRE_e + \varepsilon_{ie}\right) \quad (2)$$

[26] Continuation patent applications are new applications that allow applicants to seek new claims based on inventions disclosed in previous "parent" applications that have not yet issued (Righi and Simcoe 2023). The continuations share the parent's expiration date.
[27] Considering the above-stated construction of the 9-year event window, we thus focus on biologics whose primary patent expires between 2015 and 2021, allowing us to track post-2010 patent filings throughout the entirety of the relevant windows. The event-time patterns we present are robust to including drugs with primary patents expiring pre-2010; however, not surprisingly given the weakened incentives pre-2010, the magnitudes of the findings are less pronounced. Ultimately, there are only a small number of drugs (12) that could serve the basis for a pre-2010-only analysis, limiting the power to formalize a test of a weaker primary-patent-expiration response in the pre-2010 period.
[28] Our results are virtually unchanged when estimating Ordinary Least Squares specifications, as we show in Figure A8 of the Online Appendix.

where e indexes the treatment-event time and i the biologic. $EXPIRE_e$ represents a dummy variable (for each event time, e) capturing the event-time associated with the incidence of the treatment drug's primary-patent expiration. Drug fixed effects are captured by δ_i.[29]

We present estimates of the β_e coefficients in Panel A of Figure 4. Consistent with the predictions of the strategic-timing behavior set forth above, we find a precipitous increase in non-continuation patent filings as we near the expiration of a drug's primary patent, followed by a sharp decline upon the primary patent's expiration.

Next, we include control drugs within each stack layer. We select control drugs that are i) actively patenting by the beginning of the relevant event window but (ii) will not have a primary-patent expiration of their own until a future time at least 8 years outside of the event window, a condition that aids in the use of "clean" controls (Deshpande and Li 2019).[30] With the stacked sample designed as such, we follow Wing et al. (2024) and estimate the following specification (including the regression weights recommended by Wing et al. 2024):

$$(3) \qquad Patent_Count_{eit} = \exp\left(\alpha + \delta_i + \gamma D_i + \sum_{e=-4}^{4} \beta_{1e} EXPIRE_e + \beta_{2e} D_i \text{ X } EXPIRE_e + \varepsilon_{ei}\right)$$

where D_i is an indicator for the treatment group and other parameters are as above. Control drugs are assigned the same event-time indicators as the corresponding treatment drugs within the relevant layer of the stack.[31] The coefficients of the interactions between these event-time indicators and an indicator for the treatment drug—i.e., the β_{2e} coefficients—represent the objects of interest. This specification is intuitive and essentially estimates a

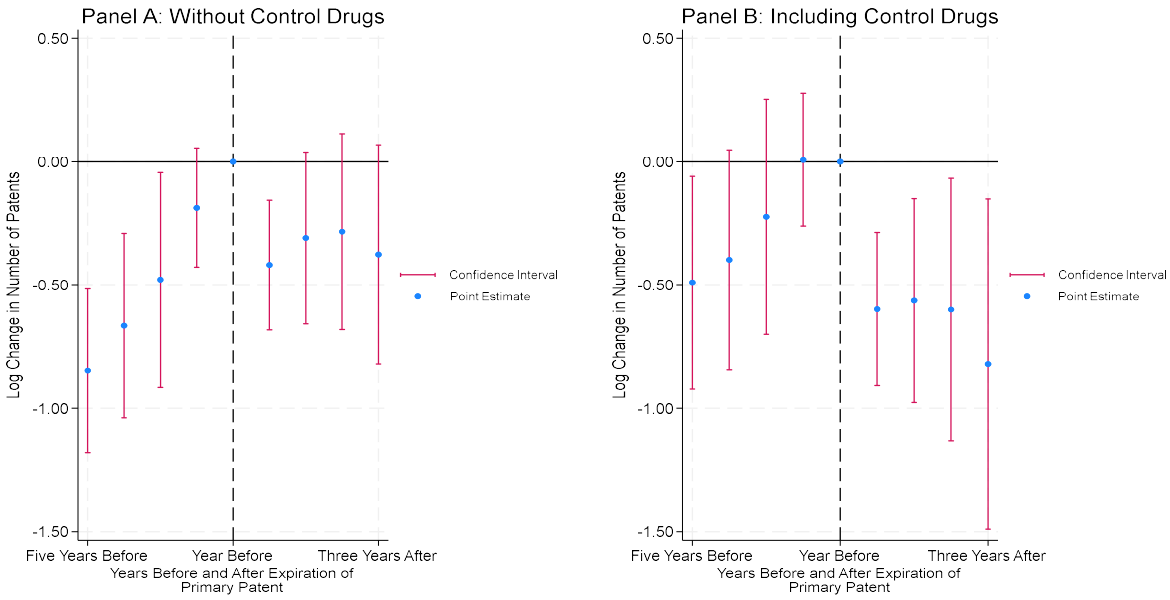
[29] In this specification and in the specification below that includes control drugs, we follow Wing et al. (2024) and Deshpande and Li (2019) and cluster standard errors at the unit level—i.e., drug level—though our analysis is robust to two-way clustering at the drug and event level.

[30] For instance, for the 2015 treatment cohort (first primary expiring in 2015), these two conditions leave us choosing a control set of drugs whose primary patent expires between 2027 and 2030. Since the essence of our exercise is one that predicts possible increasing patenting prior to the treatment event and a retreat thereafter—i.e., we predict both pre- and post-treatment effects—it is important to impose sufficient distance between the post-treatment period of our treatment windows and what would be the pre-treatment period for the control drugs' future-treatment windows. Our approach effectively imposes at least a four-year gap between such windows. However, our results are robust to alternate temporal constructions of the controls. As Panel A of Figure 4 demonstrates, our results are even robust to no control drugs altogether.

[31] Results are identical if event dummies are included, as events are perfectly identified by drug dummies and treatment status.

classic dynamic difference-in-difference-like specification within each layer of the stack—centering in event time—and then effectively averaging those estimates over all layers of the stack.[32]

Figure 4. Event-Study Specification Results: Patenting Frequency in Years Leading up to and Following Expiration of Drug's Primary Patent



Note. Panel A captures patenting data from 80 treatment drugs over a 9 year period for a total of 720 observations. Panel B includes 80 treatment drugs and 301 control drugs, also tracked over 9 years for a total of 3429 observations. 95% confidence intervals are shown in the vertical bars.

In Panel B of Figure 4, we present the estimated β_{2e} coefficients, allowing us to trace the frequency of biologics patenting for treatment drugs relative to control drugs in the years leading up to and following the year before the expiration of the focal treatment biologic's primary compound patent. The estimated pattern is highly similar to that without control drugs included. We document an increase in patenting activity leading up to the one-to-two-year period prior to primary patent expiration followed by a sharp drop in

[32] In the Online Appendix, we show substantially similar results from the Cengiz et al. (2019) specification, which tracks the same intuition but follows a slightly different specification that includes certain high-dimensional fixed effects.

patenting once the primary patent expires.[33] Moreover, the magnitudes of these swings are considerable, with the Poisson regression coefficients suggesting a nearly 40% increase in patenting frequency in the four years leading up to the year prior to primary-patent expiration followed by an over 50% fall upon expiration.

Altogether, these findings are more consistent with the strategic-timing model set forth above. Even if we allow development activity to evolve with discrete jumps over time in the non-strategic, traditional-patenting model, the timing of the relevant jumps we document align precisely with the incentivized moment in time under the strategic model.

4. Strategic Timing Analysis: Robustness Checks

As a falsification exercise, in Figure A10 of the Online Appendix, we demonstrate no clustering of patenting near primary-patent expirations in the case of continuation patents, based on the timing of when the continuation patent application is filed. Again, continuation applications have no immediate impact on the patent term of the relevant drug given that they share the priority/expiration date of their parent patents. Accordingly, one would not expect firms to file continuations at specified moments in time in a direct attempt to extend the drug's patent life.

Further, in Figure A12 of the Online Appendix, we demonstrate that the findings from Figure 4 are robust to dropping 22 treatment events whereby the relevant drugs also experience the end of the 12-year FDA market-exclusivity period during the primary-expiration event window (a regulatory exclusivity feature discussed in Part VI below).

5. Strategic Timing Analysis: Heterogeneity across Patent Type

In Table A1 and Figure A11 of the Online Appendix, we explore this strategic-timing inquiry by patent type. We find the strongest evidence of strategic evergreening

[33] The rise in patenting continues to the 1-2 year period before primary-patent expiration even though some of those filed in those final moments will not issue until after the primary-patent expiration. This does not mean that firms are necessarily sacrificing their goal of ensuring no temporal gaps in patent coverage. After all, firms are filing multiple patents leading up to primary expiration, including patents filed at 2-plus years prior. Firms are likely viewing patents in probabilistic terms and building a thicket of patents in this pre-expiration period, taking the process as late as possible up to primary expiration. With respect to those patents filed at the very end of this pre-period, we also note that firms may simply be trying to signal this evergreening strategy to competitors even if those final patents may issue after primary expiration.

with respect to device patents and then next with formulation and manufacturing patents. This heterogeneity is intuitive. A firm will be more likely to time innovative activity to occur by a particular date the more certain it is that they may be able to complete such activity by that time. Such certainty is arguably less likely to exist for innovations associated with the molecules themselves or with the clinical indications of such molecules. However, it is arguably easier to make modifications to existing devices and attempt to patent this development by target dates.[34] Accordingly, these heterogeneous findings lend confidence to an interpretation of the evergreening findings depicted thus far as being strategic in nature.

We note that this heterogeneity in strategic timing across patent types aligns with heterogeneity we also document across types in the preliminary analyses from Part IV. For instance, consider a version of Figure 3 across patent type, which we depict in Figure A7 of the Online Appendix. Again, this figure shows the difference in years between a patent's expiration and the expiration of the associated drug's first expiring patent. We likewise find that this extension is strongest among device patents (17.9 years), formulation patents (13 years), and manufacturing patents (12.6 years) relative to main-compound patents (9.9 years) and method of treatment patents (10.7 years). Similarly, consider Figure 1, where we explore how Congressional creation of the biosimilar threat leads to an increase in patenting for existing drugs. We likewise find the weakest impact of the BPCIA on the rate of main-compound patenting and the strongest response in the case of devices (see Figure A4 of the Online Appendix).

B. Innovativeness of Strategically Timed Patents

1. Innovativeness Analysis: Overview

An important feature of the traditional-patenting / non-strategic model is that the patents used to justify the research and development are associated with true innovations—i.e., novel, nonobvious leaps over the prior art. Patenting is socially harmful to protect "innovations" that are non-novel and/or are obvious extensions of existing technologies, as

[34] This claim is supported by studies that have found weaker legal validity (weaker indications of novelty and non-obviousness) for secondary relative to primary drug patents (Kyle 2016).

the promise of monopoly rents ostensibly was not needed to incentivize their creation in the first place (Frakes and Wasserman 2023). With this in mind, we turn now to test for a second marker for strategic patenting by biologics manufacturers: the collection of non-innovative secondary drug patents.

We layer this analysis on top of the above strategic-patenting inquiry. We specifically ask the following: are those secondary patents that are strategically timed to be filed just before the primary-patent expiration of lower levels of innovativeness? That is, are manufacturers taking an even easier path towards achieving evergreening goals by taking advantage of limitations of the Patent Office to screen innovative from non-innovative applications? We label behavior of this nature "non-innovative gaming" on the part of biologics manufacturers.

2. Innovativeness Analysis: Methodology and Results

To shed light on the existence of non-innovative gaming, we require empirical markers of patent innovativeness. For these purposes, we primarily follow a series of recent studies (Frakes and Wasserman 2023, Lei and Wright 2017, Frakes and Wasserman 2017; and Lemley and Sampat 2012) and exploit the fact that innovators often file for patent protection both at the U.S. Patent Office and the European Patent Office (EPO). The EPO has similar patentability standards to the U.S., including with respect to novelty and nonobviousness requirements, but invests substantially more resources per application (including examination time allotments and examiner compensation) and works in examination teams (Picard and van Pottelsberghe de la Potterie 2013; Chien 2018). Accordingly, to draw on a signal on the novelty and non-obviousness of innovations associated with U.S. patents, we assess whether a given innovation's "twin" patent application at the EPO is allowed.

For these purposes, we draw on administrative data compiled by the OECD, which collects data on innovations associated with patent applications filed at both world offices and tracks associated outcomes. Roughly 76% of the 11,595 drug-patent pairs in our dataset are associated with patent filings at the EPO, easing external validity concerns. To assess the innovativeness of those patents filed in the period surrounding the primary patent

expiration, we then estimate a version of specification (3) that uses as the dependent variable the incidence of the focal U.S. patent having a twin application that is allowed at the EPO.

We confront a truncation challenge, however, as we need to allow time for the EPO to reach its patentability decision, which takes up to five years.[35] As demonstrated by Table A2 of the Online Appendix, the incidence of EPO allowance of U.S. biologics patents begins to fall notably after the U.S. patent filing years of 2016 and 2017, suggestive of truncation issues materializing around this time. Accordingly, we aim to focus on event windows that end in 2017. Given this restriction and the need to focus on post-2010 patents, we narrow the breadth of our observation windows. We begin in Panel A of Figure 5 with a narrower window that does not sacrifice length on the pre period—i.e., we estimate a specification that includes only pre-primary-expiration event dummies and the contemporaneous primary-expiration dummy for the 2015-2017 primary-expiration cohorts (with control drugs). In Panel B of Figure 5, we focus our event window on post-primary-expiration years. In particular, we estimate a specification that includes the one-year pre-period dummy as the reference period and includes all future event dummies through three years post expiration, doing so for the 2011-2014 primary-expiration cohorts (again with control drugs). We note upfront that our analysis is robust to alternative approaches to addressing these truncation challenges—as we demonstrate in the Online Appendix.[36]

Focusing first on Panel A of Figure 5, we find that indicators of innovativeness among filed biologics patents increase as the patent expiration of the drug's primary patent nears. However, in the year before that expiration, there is a precipitous drop in the innovativeness indicator. As both Panel A and Panel B of Figure 5 demonstrate, after this dip, we find a return to the elevated EPO allowance rate once the primary patent expires. The elevated innovativeness of those patents filed the year of expiration may be a spillover

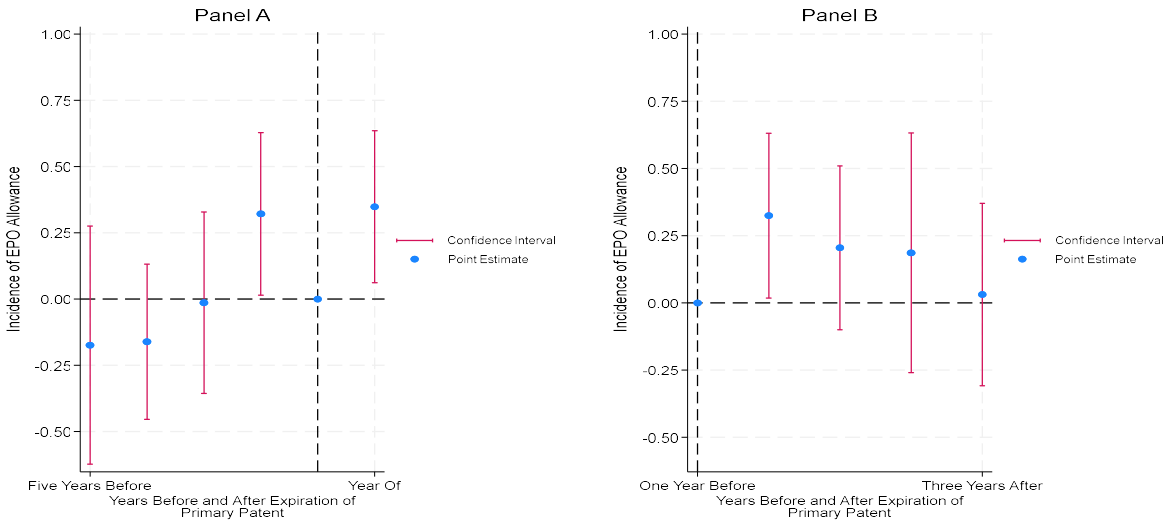
[35] See https://www.epo.org/en/service-support/faq/applying-patent/procedure/how-long-does-grant-procedure-take#:~:text=The%20European%20patent%20grant%20procedure,date%20your% 20application% 20is%20filed.

[36] Such alternative approaches include (i) focusing on a two-year window on either side of the year-prior reference period, (ii) estimating specifications that include pre-2010 primary expiration cohorts, and (iii) estimating specifications that include patents filed past 2017 (relying on an assumption that truncation concerns equally affect treatment and control drugs).

of the quality of research activities undertaken in the years leading up to pre-primary-expiration year. In this light, the dip in EPO allowance rate in the year prior to the primary expiration may not reflect mere mean reversion in the quality of research activities, but rather a conscious filing of lower-quality patents for strategic purposes. As demonstrated by Panel B, that more natural point of mean reversion where research quality lightens up after the surge suggested by Panel A begins in the year after primary-patent expiration.

Interestingly, these findings are consistent with *both* the non-innovative gaming story and its alternative where firms are strategically timing legitimate innovations on secondary features. In particular, our results suggest a story in which firms increase their research and development in the years leading up to the primary patent's expiration for the relevant drug, producing secondary drug features with greater and greater markers of innovativeness. However, right at the final moment before the primary expires, firms may be supplementing their evergreening strategy with a set of non-innovative patents.

Figure 5. Incidence of EPO Allowance Among US Biologic Patents Filed in Years Leading up to and Following Primary-Patent Expiration



Notes: this analysis presents results from a version of specification (3) that uses as the dependent variable the incidence of the U.S. patent application also being allowed at the EPO (among a sample of applications also filed at the EPO). Specifications in each panel include treatment-drug cohorts allowing for the event window to track applications filed starting at least in 2010 and through 2017. There are 33 treatment drugs in Panel A and 38 in Panel B. N = 283 in Panel A and 356 in Panel B.

3. Innovativeness Analysis: Robustness Checks

As discussed in the Introduction, one of the key motivations to build patent thickets is to protect against the possibility that issued patents will be invalidated by the courts—e.g., on lack-of-novelty grounds. A key mechanism firms may use to build thickets is the filing of a continuation patent, which again refines the claims of a prior "parent" application without changing the innovation itself (Carrier and Tu 2024; Tu et al. 2023; Righi and Simcoe 2023). Thus, we predict that if firms file less innovative patents in the year prior to the primary-patent expiration—as Figure 5 implies—they will be more inclined to build a thicket around those low-quality patents by making them parents of continuation patents. These hypothesized continuation patents will be filed at later dates, but they nonetheless share a priority and expiration date with their parent patent. Accordingly, while filing continuation applications by the primary-patent-expiration date does not *directly* lengthen the patent life of the relevant drug—a point which was the basis of the falsification check above—such filings may nonetheless *indirectly* serve evergreening goals. We find evidence consistent with this prediction in Figure A17 of the Online Appendix.

Further, in Figures A18-19 of the Online Appendix, we consider a final, albeit imperfect, innovativeness metric, whereby for the patents filed in the event window surrounding the primary-patent expiration, we consider the semantic similarity between that patent and its nearest semantic neighbor. The results from that exercise document a sharp drop in this similarity measure at the primary patent expiration, consistent with less novel patents being filed in the pre-primary-expiration period and thus consistent with the non-innovative gaming model described above.

C. Concluding Thoughts Regarding Strategic Evergreening and Thicketing

All told, our analysis finds suggestive evidence that firms are filing secondary biologics patents in a manner that maximizes the amount of time over which patents protect some aspect of the relevant drug, which may serve various entry-deterring and entry-blocking goals. Moreover, we find suggestive evidence that some of those secondary patents filed for such purposes are of more questionable legal validity.

VI. Relationship between Patenting and Biosimilar Entry/Threat

The evidence of thicketing and evergreening set forth above demonstrates the potential for biologics patent portfolios to meaningfully forestall competition from biosimilars. In this Part, we discuss whether this potential, in fact, materializes. Primarily, we consider several descriptive observations about biosimilar entry, which are generally suggestive—though not determinative—of a meaningful blocking effect.

First, despite over 500 original therapeutic biologics having been approved by the FDA, only a small number of biosimilars have entered the market to date in the U.S. Seventy-one biosimilars have been approved by the FDA covering 20 reference (original) biologics. Out of those 20, only 16 have experienced market launch by the relevant biosimilar(s) as of June 2025.

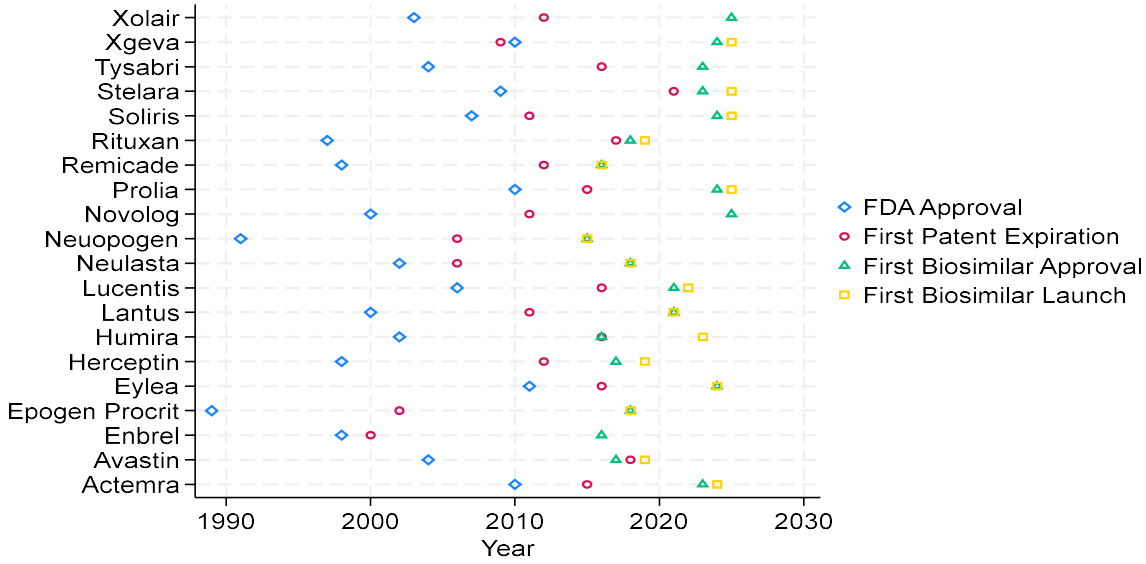
Second, as demonstrated by Figure 6, among those small number of drugs with biosimilar entry to date, the timing of biosimilar entry comes on average over 8 years after the first expiring patent of the brand, suggesting a possible role for patent-induced delays stemming from the follow-on patenting activity explored above. Third, biosimilar market launch sometimes occurs years after the FDA even approves biosimilar market entry. When this occurs, it is generally due to settlement negotiations or judgments surrounding patent disputes between the sponsor and biosimilar manufacturers. Consider, for instance, the brand Enbrel, which experienced its first associated biosimilar approval in August of 2016. Despite this regulatory approval, court rulings surrounding certain Enbrel patents have precluded market entry to date, with biosimilar launch not expected until certain Enbrel patents expire in 2029.[37]

Fourth, among those biologics that have experienced a launch of a competing biosimilar, we consider their effective market life—i.e., the time between the biologic's original FDA approval and the market launch of its first biosimilar competitor. This amount is 18.4 years on average, spanning from 13 to 29. Moreover, this amount is arguably an underestimate as many drugs have yet to experience biosimilar approval and

[37] See https://www.fiercepharma.com/pharma/amgen-stalls-samsung-s-enbrel-biosim-until-2029-second-patent-win-year.

others such as Enbrel will be waiting an additional set of years before biosimilar launch. Notably, the effective market life of a given biologic is larger than the roughly 12-14-year corresponding amount for the small molecule marketplace, a marketplace characterized by substantially weaker degrees of patent thicketing and evergreening.

Figure 6. Biosimilar Entry Timelines, Among Biologics Experiencing Associated Biosimilar Approval to Date



Notes: relevant dates are for those twenty original, sponsor biologics experiencing an approval of an associated biosimilar as of June 2025.

It may be premature, however, to draw strong inferences from this modest entry to date and from the patterns depicted in Figure 6. After all, the biosimilar product space itself is rather new, with the first biosimilar being approved in 2015 and a quarter of them being approved in 2024 alone. A more fundamental challenge is that alternative theories may explain this limited entry. First, the costs of receiving FDA approval to enter the market as a biosimilar—i.e., roughly $100-$250 million—may alone be enough to deter entry (Atteberry et al. 2019, Feng et al. 2024). Second, new biologics manufacturers receive a statutory, non-patent-related twelve-year period of exclusivity before the FDA

will approve entry of a biosimilar. After that twelve-year period ends, it may be uncertain whether a viable market still exists for patents to have a marginal effect.[38]

Ultimately, the delaying effects of biologics patent portfolios on biosimilar entry is an empirical question, but one that is difficult to test as there is no straightforward way to construct a counterfactual without the biologics patent portfolios. Nonetheless, we at least reiterate that our analysis from Part IV has demonstrated that the amassing of these patent portfolios in the first place was caused by the *threat* of biosimilar entry.

VII. Discussion and Policy Analysis

Congress is presently considering proposals aimed at curbing thicketing and evergreening by biologics manufacturers. For instance, the Affordable Prescriptions for Patients Act (APPA), which was unanimously passed by the U.S. Senate in 2024 and reintroduced to the U.S. Senate in spring of 2025, aims to address high drug prices by limiting the number of patents that may be litigated in a patent infringement lawsuit between a biologics manufacturer and a biosimilar applicant for those patents that were filed four-plus years after the drug is approved by the FDA.

In the Online Appendix, we offer additional details on the APPA and then use our novel biologics patent database to simulate the proposed law's reach. We demonstrate that the APPA would prevent roughly 5% of the average drug patent portfolio from being asserted in litigation. Further, it would impact at least one patent for 13.7% of the drugs in our database and more than 20 patents for 5.5% of biologics. We also demonstrate how these impacts would change (assuming no manufacturer responses) if the APPA were to modify the associated time cut-offs—e.g., restricting manufacturers from asserting patents in litigation that were filed at all after the FDA approval for the drug, a modification which would then leave roughly 55% of the patents in an average biologics patent portfolio unavailable for assertion in litigation.

[38] This latter point may be less of a concern for those drugs depicted in Figure 6, where market entry has generally occurred years past loss of FDA exclusivity. However, for smaller-market biologics, this concern remains. We also note that the marginal effect of evergreening practices may be limited for the reasons set forth in Part III. If a firm receives a patent on a new drug feature, it is possible for biosimilars to enter the market under an older version of the drug. While we indicated the real possibility of spillover effects across these different drug products—a possibility informed by much litigation and other legal attention paid to product hopping—the extent of such spillover effects ultimately remains an empirical question.

The welfare implications of our above findings—in addition to the simulated impacts of the APPA—are rather nuanced. As discussed in Part V, some of the secondary patenting that firms may be pursuing in order to lengthen the patent lives of their drugs are of questionable innovativeness. Accordingly, those patents may contribute to the deadweight losses (and consumer-surplus losses) associated with the exclusionary effects of patents without providing commensurate innovation-inducing benefits, in which case curbing them through policies like the APPA may be welfare-enhancing.

On the other hand, our findings in Part V do suggest that some of those strategically timed secondary drug patents represent novel, and non-obvious innovations. However, even those innovative patents may bring some offsetting welfare losses. As discussed in Part III, they may be part of a broader product hopping/shifting strategy that potentially blocks entry on earlier drug versions that lack the relevant secondary drug feature. The shifting of the consumer base from the old to the new version of the drug may not simply be a reflection of a competitive market's adoption of a superior drug product. Rather, in executing this shift through campaigns aimed at physician buy-in of new drug versions, manufacturers may be taking advantage of certain market failures, mainly imperfect physician agency and moral hazard in drug coverage (Carrier and Shadowen 2016).

Though federal antitrust jurisprudence has embraced that such behavior may pose anticompetitive harms,[39] caselaw has also expressed that whether these practices are pro- or anti-competitive is a case-specific inquiry that depends, among other things, on the nature of the coercive conduct employed (Carrier and Shadowen 2016). The APPA—which Congress has stated aims, in part, to curb product-hopping practices—elects to depart from the case-by-case approach of antitrust law and apply the same litigation-enforcement restrictions on all manufacturers. Ultimately, for the same reason that the antitrust courts take a case-by-case approach, we face challenges in our ability to precisely isolate and calculate the aggregate welfare losses associated with the strategic patenting components to evergreening practices. Instead, in considering the policy implications of our analysis, we aim more modestly to shed light on the potential reach of the APPA and

[39] See, e.g., New York ex rel. Schneiderman v. Actavis PLC 787 F.3d 638 (2d Cir. 2015).

similar proposals and to validate—throughout our empirical analyses above—that the foundations for competitive harms are present in the biologics marketplace.

Finally, we note that, should policymakers only wish to target evergreening practices that utilize non-innovative patents, policies such APPA may overreach given that our analyses also suggest the existence of a number of innovative secondary patents. Other policies—such as those that give examiners more time or resources to search for prior art—may be better suited for this goal in that they aid the Patent Office in screening out non-innovative biologics patent applications (Frakes and Wasserman 2023).

VIII. Concluding Thoughts

We build the first known database of all patents associated with large-molecule drugs, the fastest growing and now highest-revenue-generating sector in the pharmaceutical market. Helping to illuminate why biosimilar entry is so delayed and why biologics manufacturers' prolonged earnings are so high, we document evidence of strategic patenting practices by manufacturers, whereby they obtain a large number of patents per drug, many of which are strategically timed to prolong the period over which patents protect the relevant drug and some of which are of questionable innovativeness. We also document a range of empirical markers suggestive of the effect of such strategies on competitive entry.

A final complication to understanding the welfare implications of these findings stems from the possibility that drug manufacturers may only be willing to develop new drugs / new molecular structures if they use strategic patenting to maximize the rents associated with their drug products. In other words, the receipt of patents on non-novel and/or obvious secondary drug features and/or the returns from product-hopping and related strategies may be needed to subsidize innovative new drugs in the first instance. This may be due to certain imperfections in the design of the patent system—e.g., suboptimal patent terms (Budish et al. 2015). Accordingly, might new-drug innovation fall if Congress adopts policies that will target strategic practices?

The link between new drug developments and expected drug market sizes / returns has been the subject of a large literature in economics.[40] The elasticities of innovation to expected market size estimated by this literature range considerably—e.g., from as low as 0.2 to as high as 4. Nonetheless, recent studies have come out on the low end of this range (Dubois et al. 2015; Chen et al. 2025); moreover, other studies have found that the marginal patents discouraged from lower expected returns are less innovative (Gilchrist 2016; Dranove et al. 2020).

Accordingly, recent work suggests that a reduction in expected market size stemming from policies like the APPA that aim to curb thicketing and evergreening would not substantially impact the development of new biologics. Nonetheless, the literature has not reached a full consensus on these questions and has mostly focused on the small-molecule marketplace. Ultimately, it is beyond the scope of this paper to answer how biologics manufacturers would respond in their innovative activities moving forward to policy initiatives aimed at reducing the kinds of strategic patenting practices that are the focus of this paper. Rather, this paper again approaches this discussion from the perspective of giving policymakers and commentators insights into the nature of the patenting tools used to exclude competitors, which may prove useful to policymakers who do arrive at the decision to promote earlier biosimilar entry in order to reduce drug prices.

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