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# STRATEGIC PATENTING: EVIDENCE FROM THE BIOPHARMACEUTICAL INDUSTRY

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## ABSTRACT

Biological drugs account for just two percent of prescriptions filled in the U.S. but fifty percent of prescription-drug spending. To explore the role patents play in explaining high biologics prices, we build the first comprehensive database of patents associated with all FDA-approved biologics. We first establish that much of what drives biologic patenting is the desire to block entry by competing biosimilars. For these purposes, we estimate the response to a 2010 Act that created an abbreviated pathway for biosimilars to receive FDA approval. We then document robust evidence consistent with two patenting strategies that may block biosimilar competition: thicketing and evergreening, whereby firms supplement primary patents with a dense web of later-expiring patents on secondary drug features. We conduct various exercises to suggest that these behaviors are undertaken with exclusionary purposes that go beyond the traditional justifications of the patent system. We then set forth various descriptive statistics surrounding biosimilar entry to suggest that these patenting strategies are, in fact, effective at delaying biosimilar entry. Finally, we simulate the degree to which biologics patent portfolios are impacted by policy proposals currently under consideration to address thicketing and evergreening.

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## I. Introduction

In the United States, prescription drug spending exceeded $800 billion in 2024 (Tichy et al. 2025), accounting for nearly 2.7% of the U.S. gross domestic product.[1] Patents are thought to play a key role in explaining this spending, offering firms the potential to exclude competitors from the market. Of course, monopoly rents are a key purpose of the patent system, with the promise of such rents encouraging investments in research and development in the first place (Nordhaus 1969). However, there is a growing concern that brand-name manufacturers are strategically engaging in patenting practices that allow them to benefit from periods of exclusivity in excess of socially desirable levels (Frakes and Wasserman 2023).

To begin to understand strategic drug patenting, it is first important to acknowledge that most drugs are not simply associated with a single patent on the underlying molecule. Rather, manufacturers acquire multiple patents per drug, particularly with respect to "secondary" drug features, such as routes of administration, methods of use, devices, and manufacturing processes. One notable patenting strategy that draws on secondary patenting is known pejoratively as "evergreening," whereby a pharmaceutical firm seeks secondary patents years after filing the primary patent (Kesselheim and Avorn 2006; Hemphill and Sampat 2013). Given that patent terms run twenty years from filing, these later-filed patents extend the period over which the drug faces patent protection. Relatedly, firms may engage in patent "thicketing," whereby they build a dense web of patents for each drug to ensure that at least some patents in the portfolio survive legal challenges (Lemley and Shapiro 2005; Hall et al. 2021) and/or, generally, to compound litigation- or licensing-related expenses for competitors wishing to navigate the associated web of patents.

[1] This amount may not reflect manufacturer rebates. An analysis of National Health Expenditures Accounts data for 2023 reveals U.S. retail prescription drug spending in that year of roughly $450 billion. This amount is net of rebates but captures retail spending only (Martin et al. 2024).

Drawing from cases 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." 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—e.g., penicillin. 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 (Association for Accessible Medicines. 2019), spending on biologics represents close to 50% of net drug spending, a share is expected to increase in the years to come (IQVIA 2023).

Why do we know so little about biologic patents? The answer, in part, relates to the regulatory structure surrounding these markets.[2] U.S. law has mandated since 1984 that brand-name manufacturers of small-molecule drugs disclose their associated patents to the Food and Drug Administration (FDA), which publicly disseminates the resulting patent lists in something

[2] 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.

known as the Orange Book.[3] The law works quite differently for biologics. The disclosure requirements for biologics patents are quite limited, with our analysis demonstrating that such requirements only capture less than 4% of the patents associated with approved biologics.

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 conduct structured searches of 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). The resulting database consists of 11,595 drug-patent pairs.

Using these data, we begin our investigation into strategic patenting by first establishing a connection between the patenting of biologics and the exclusionary impulse of manufacturers. Data-availability aside, confronting questions of this nature has been challenging for the literature as it is not straightforward to link patents to specific, potentially infringing products and to find plausibly exogenous shocks in the competitive space surrounding such products (Righi and Simcoe 2022). In our case, we take advantage of an opportunity afforded to us by Congress in 2010 when it passed the Biologics Price Competition and Innovation Act (BPCIA), which created an abbreviated pathway for FDA approval of biosimilars. We find that the creation of the biosimilar threat led biologics firms to accelerate the degree to which they sought patents on existing biologics, with no corresponding acceleration in the case of existing small molecules.

[3] 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).

We then focus this strategic-patenting inquiry on the question of thicketing and evergreening by setting forth certain descriptive statistics surrounding the patent portfolios that we uncover. Biologic drugs 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 the expiration date 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.

We next explore whether these preliminary markers of thicketing and evergreening can be explained by behaviors that meet the more specific definition of "strategic" customarily set forth by the patent literature. This definition generally captures scenarios where a patent is acquired for exclusionary purposes that go beyond the traditional welfare-enhancing rationale of fostering the innovation associated with the specific patent (Blind et al. 2006, Moser 2013). Guiding our inquiry here are the following two questions, which probe whether biologics firms' secondary patenting motivations extend beyond simply justifying the specific secondary innovation. First, by filing patents on new drug features before earlier patents associated with the drug expire, are firms using secondary patents as a part of a broader business strategy aiming to block biosimilars from entering the market under both new *and old* versions of the drug? Second, are manufacturers taking advantage of certain institutional features of the U.S. Patent & Trademark Office (Patent Office) to acquire non-innovative secondary patents that further exclusionary goals?

We shed light on these two questions through a range of empirical exercises. For instance, we first test for evidence of strategic timing of secondary patenting. We theorize that firms seeking to maximize evergreening goals will make sure to secure new patents prior to the expiration of

previous patents and as close as possible to the expiration of preceding patents. Estimating event-study specifications (following Wing et al. 2024 and Cengiz et al. 2019) in the window around the most salient preceding patent—the primary compound patent associated with the drug—we find evidence suggestive of such timing. Moreover, we then use various markers of the novelty and nonobviousness of patent applications and find evidence that some portion of those patents filed just before the primary patent's expiration are of questionable innovativeness.

Altogether, these findings suggest that biologics patent portfolios have the potential to meaningfully forestall entry by biosimilar competitors. Whether such an effect will occur in practice is theoretically ambiguous. After all, the high cost of developing a biosimilar and receiving FDA approval to enter as a biosimilar—upwards of $100-250 million—may be enough to deter entry. To begin to shed light on the blocking effect of biologics patenting practices, 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-plus-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, as opposed to compound and method of treatment patents.

Congress and the Patent Office have recently proposed various reforms aimed at curbing evergreening and patent thicketing practices. In a final exercise, we simulate the extent to which these various 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-VI, we explore the strategic patenting behaviors of biologics manufacturers. In Part VII, we explore the association between these patenting practices and biosimilar entry. In Part VIII, we explore the potential of certain policies aimed at reducing biologics patent thickets. In Part IX, we conclude.

## II. Background

### A. Literature Review

Of closest relevance to our analysis are a series of studies utilizing Orange Book data disseminated by the FDA 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.[4]

[4] The closest the literature has come to showing comparable statistics for biologics comes 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 VI and VII.

Beyond our specific contributions to the pharmaceutical patenting scholarship, our analysis makes various advancements to the broader strategic patenting literature. As above, strategic patents are those filed for exclusionary reasons that go beyond solely protecting the legitimate innovation underlying the patent from imitation. Patents meeting this definition are potentially problematic from a welfare perspective to the extent they forestall competition while being tangential, or even counter, to the fostering of innovation.

The literature has taken various approaches to documenting the existence of strategic patenting. A common theme across many of these approaches is to estimate correlations 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 reflective of strategic patents.[5] Hall and Ziedonis (2001) documents a growing disconnect between firm-specific patenting volumes and research and development expenses, particularly with respect to firms with sunk, pre-existing capital intensity worth protecting through patent-based exclusionary practices.[6]

Several aspects of these studies leave them falling 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

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

and Ouellette 2023). More broadly, citation-based approaches are limited by attempting to infer strategic motivations behind patenting based 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. As with the above studies, we explore the connection between patenting practices and metrics of innovation. However, we go beyond that suggestive exercise and 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.[7]

Our analysis is also related to a set of studies exploring the impacts of firm patenting on the associated marketplace, including studies exploring the impacts of patenting on cumulative innovation (Sampat and Williams 2019, Galasso and Schankerman 2015)[8] and the impacts of patent disclosure on follow-on innovation (Hedge, Herkenhoff, and Zhu 2023). In addition, our analysis is related to a literature exploring the connection between innovation and competition in the pharmaceutical industry.[9] Considering that one of the foundations for the strategic use of non-innovative patents is a patent office with imperfect patentability screening, our research also builds

[7] Our methodological approach is closest in spirit to that taken by Righi and Simcoe (2023). Righi and Simcoe are likewise able to link patents to specific product spaces—in their case, specific technology standards—and likewise explore how patenting practices change in response to a shock in the relevant competitive environment. Specifically, they explore the impact of the relevant standard being published. After this time, they find evidence that firms opportunistically file continuation patents to modify the claims of parent applications that were filed before the standard publication, where these claim modifications ensure that the claims cover the newly published standard.

[8] See Hall et al. (2014) for a review of the related literature.

[9] See Cunningham et al. (2021) for a recent literature review. Cunningham et al.'s own analysis explores how incumbent pharmaceutical firms' acquisition activities block future drug-product competition.

on a line of studies that have explored the determinants of elevated grant rates at the Patent Office (Jaffe and Lerner 2004; Lemley and Sampat 2012; Frakes and Wasserman 2017).

### B. Background: Pharmaceutical Regulatory Approval Process

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. Whether the generic receives FDA approval also turns on the status on the relevant patents held by the brand-name firm. The HWA requires the brand 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 of 1984 did not address the approval and patenting of biologics, perhaps due to the fact that scientists did not meaningfully begin to develop biological drugs until the 1970s. 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.[10] However, for reasons 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), we focus our analysis on therapeutic biological drugs rather than vaccines, leaving the latter for the subject of future study.

[10] 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."

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 likely 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.

Indeed, this discussion is of relevance as 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. 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 (and thus infringement) 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—i.e., an abbreviated approval pathway is not possible—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 patent 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*. We acknowledge that 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 is likely doing little direct work to discourage Firm C's entry in Scenario 3. What is likely to block Firm C from entering this Crohn's market is not the threat of a patent infringement suit from Firm A, but instead the considerable expenses needed to conduct the relevant clinical trials showing safety and efficacy of using the relevant drug to treat Crohn's. Firm C is unlikely to undertake these expenses as (i) Firm C, by assumption, is not the party holding the relevant patent and thus lacks the ability to exclude biosimilars from competing against its new Crohn's biologic and (ii) Firm C cannot prevent physicians from prescribing Firm A's Drug X off-label for the treatment of Crohn's.

Putting this all together, to focus our attention on those biologics patents that may meaningfully forestall competition, we focus on those patents that are specifically relevant to *biosimilar* infringement. Moreover, to recap the point of the above demonstrations, when patents claim drug features that require FDA approval—e.g., new indications, routes of administration, etc.—and when the FDA has not approved such features, we exclude such patents.[11] On a final note regarding the reasonableness of these inclusion choices, our decisions track those taken by Congress in calling for the construction of the Orange Book in the small-molecule context.

### B. Search Process

To identify biologics patents meeting this criterion, we follow these steps: (1) identify patents listed in the FDA's Purple Book, (2) identify patents asserted in litigation in the United States (including a Patent Trial and Appeal Board proceeding) in relation to any FDA-approved therapeutic biologic, (3) identifying patents that received a patent term extension under 35 U.S.C. §156, which is designed to restore patent term lost during the FDA's review process, and (4) conduct structured patent searches utilizing Orbit Intelligence patent analytic and search software (discussed further below). The vast majority (over 90%) of the biologics patents that we identify are produced through the last search-based step.

A key challenge in implementing this search is that public 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

[11] For similar reasons, if the FDA had only approved the biologic drug alone, we did not include combination patents that claimed an FDA-approved biologic to be used in combination with another chemical compound.

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. That is, in a first stage, we start with a narrow framing of one parameter—mainly, limiting the search to corporate entities[12] 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.[13] Reading the patents identified by this search allows us to further narrow down to the specific patents associated with the given biologic. 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. Finally, we search for patents that contain the biosequence of the relevant biologic. In the Online Appendix, we discuss other aspects of the resulting searches and provide greater detail regarding this staging process.

[12] Specifically, we limit the search to corporate entities and any subsidiaries thereof who filed for FDA approval and/or where involved in the development, manufacture, or marketing of the biologic, as we discuss in greater detail in the Online Appendix.
[13] This first stage is slightly different with respect to a search for device patents as we discuss in the Online Appendix, a search that requires a review of the full text of the patent document.

We emphasize that this protocol is designed to capture the full scope for patenting associated with each biologic. As discussed in the Introduction, originating firms may seek patents on the active compounds, routes of administration, associated devices, methods of treatment, and methods of manufacturing. As part of this process, we also code each included patent for its type.

Our primary results will include pending patent applications in the associated patent portfolios.[14] 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.

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%).[15]

[14] Nonetheless, we exclude applications that have been formally abandoned with the Patent Office, as they will ostensibly never issue and have blocking effect.

[15] 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,

### 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 our analysis in this manner and instead organize our data and consequent 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.[16] By keeping our analysis of patenting behavior at the brand level, we make sure to include such hopping/shifting strategies among the scope of our strategic-patenting analysis.

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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.

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

## IV. 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 desire to block competitive entry in the first place.[17] Specifically, we test whether biologics manufacturers' amassing of patents was caused by the very initiation of the biosimilar competitive threat.

For these purposes, we take advantage of an unusual opportunity afforded by Congress in March, 2010 when it passed the Biologic Price Competition and Innovation Act (BPCIA) as a component to the Affordable Care Act. As noted above, 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. Instead, the BPCIA simply requires a showing of biosimilarity to the original, already-approved biologic.

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, for the purposes of this exercise, 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 drugs?

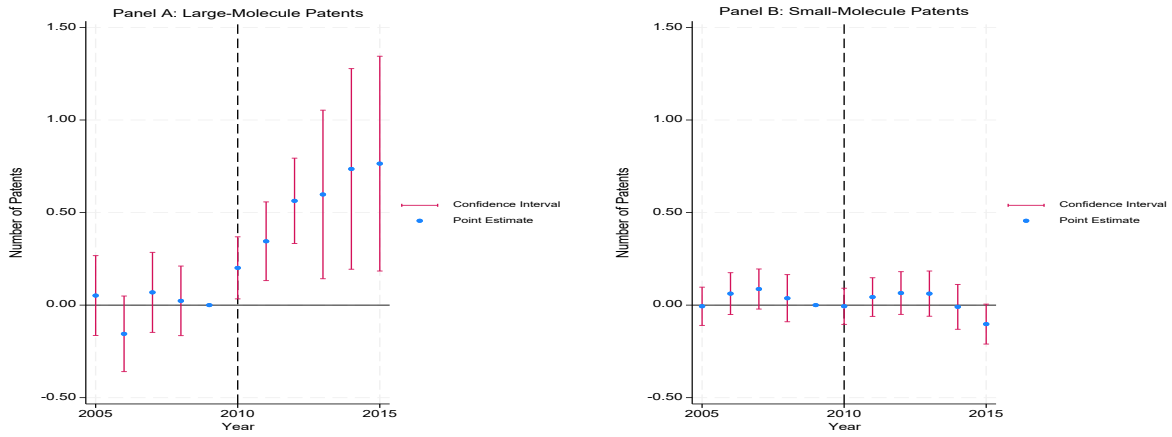
[17] At first blush, this might seem obvious; however, we note that the literature has discussed motivations to patent beyond simply desires to exclude competitors, including information-based and signaling motivations (Farre-Mensa et al. 2019, Harhoff 2009, Czarnitzki et al. 2007, Long 2002) and desires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

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 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 $\delta_i$ 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 $t$.[18] We then plot the estimated $\beta_t$ 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.

[18] 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, where the coefficients in each panel of the figure are interpreted as log changes in patent counts. Nonetheless, these interpretation points 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.

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 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 patenting volume has roughly doubled the 2009 level.

Consistent with a causal effect of the introduction of the biosimilar threat from the BPCIA, 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 formalize the comparison of the large- and small-molecule response to the BPCIA and estimate a corresponding difference-in-differences specification. The findings confirm the statistical significance of the larger biologics response.

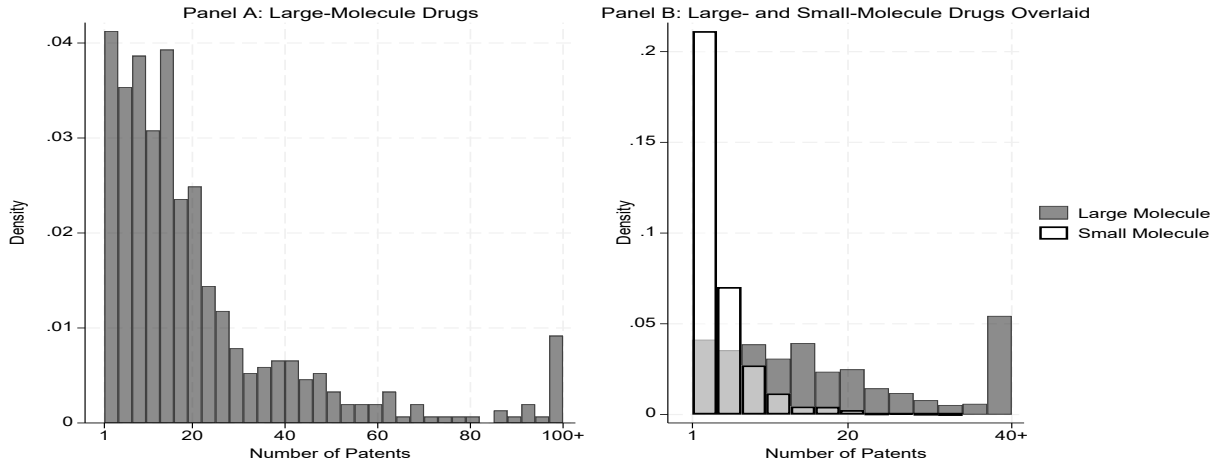
In Figure A4 of the Online Appendix, we further show responses to the BPCIA by patent type. In Part VI below, we theorize that strategic gaming of patents is less likely with respect to some patent types over others, mainly main-compound patents. Consistent with these predictions and consistent with the findings in Parts V and VI below of the weakest evergreening practices for main-compound patents, we find the weakest impact of the BPCIA on the rate of main-compound patenting. Moreover, consistent with the findings below of the strongest markers of evergreening for device patents, we find the strongest response to the enactment of the BPCIA in the case of devices. These heterogeneous effects lend confidence to a strategic interpretation of our findings.

## V. Descriptive Analysis of Patent Thicketing and Evergreening Behaviors

### A. 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

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.

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.[19] As is evident from Panel B, large-molecule drugs tend to have substantially more patents than small-molecule drugs. Whereas virtually none—less 1 than percent—of the small-molecule distribution is beyond 20 patents-per-drug, a substantial portion of large-molecule drugs—roughly 35 percent—have over 20 patents. Seven percent of biologics have more than 50 patents and 3 percent have more than 100. The average patent-per-drug of biologics is 22.7, in comparison with 3.8 for small-molecules.[20]

[19] 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).

[20] 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

Altogether, the number of patents that biosimilars need to navigate before entering the large-molecule market greatly exceeds that of small-molecule generics.[21]

### B. Evergreening

Of significance is also the degree to which patents in these dense portfolios extend the exclusivity periods associated with the relevant drugs. To begin to show this, we calculate the difference in years between the first- and last-expiring patent for each biologic and then, in Figure A6 of the Online Appendix, show a histogram of this difference across all 509 biologics associated with at least one patent.[22] The distribution has both a substantial mean and spread. The mean gap between first and last expiring patents per drug is 17.4 years with a standard deviation of 11.4 years. Nearly 40% of biologics have at least a twenty-year gap.

Figure A6 gives a potentially inflated sense of evergreening as it places substantial weight on just two patents—the first and last expiring—and it is possible that one of these is an outlier within the given portfolio. In Figure 3, we provide a sense of the evergreening potential of a given biologic patent itself. In particular, we organize the data at the drug-patent pair level and show a histogram of the distance in years between the focal patent's expiration and the expiration of the first-expiring patent associated with the drug. In Panel B, we overlay this large-molecule histogram with its small-molecule counterpart. Doing so, we continue to document evidence of both a high level and a high spread in the degree to which biologics patents extend the duration

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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 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.

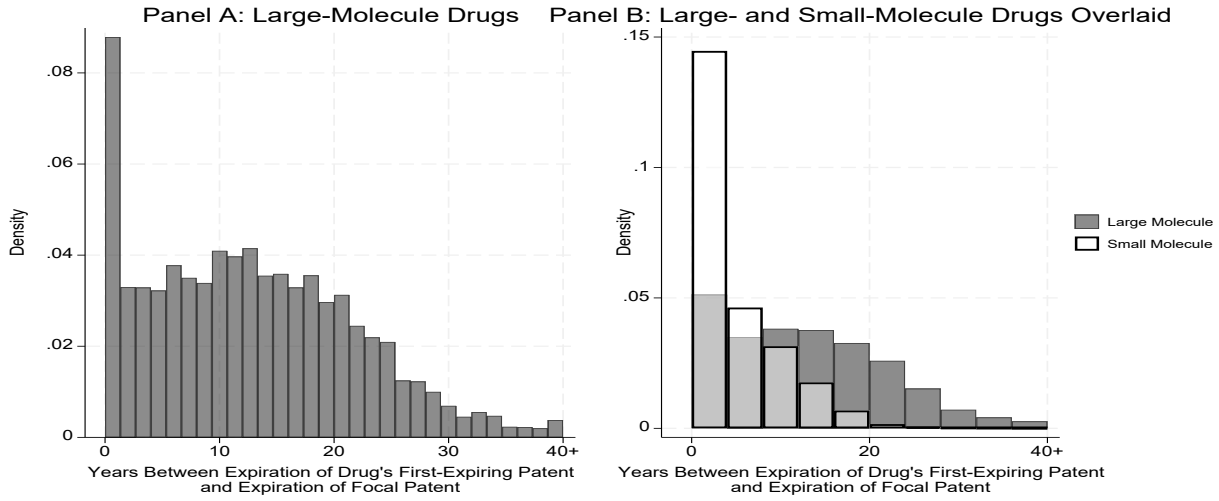
[21] In Figure A5 of the Online Appendix, we show counterparts to Panel A of Figure 2 that separately depict the distribution of patent counts across biologics by different patent types.

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

over which patents protect the relevant drug, in addition to evidence of notably stronger markers for evergreening in large relative to small-molecule drugs. For instance, 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.

In Figure A7 of the Online Appendix, we show a counterpart to Panel A of Figure 3 by patent type and demonstrate that these behaviors may extend to all types of patents, even follow-on main-compound patents. However, we do find that the average degree to which patents expire after first-expiring patents is smallest among main-compound patents (9.9 years) and method of treatment patents (10.7 years), while strongest among device patents (17.9 years), formulation patents (13 years), and manufacturing patents (12.6 years).

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.

## VI. Markers of Strategic Behavior

In this Part, we attempt to diagnose whether the evergreening markers suggested by Figure 3 are indeed reflective of strategic practices, as such term is defined in the Introduction. We approach this inquiry in two steps. In the first step, we view strategic evergreening through a slightly broader lens and ask the following question: are biologics manufacturers purposively timing their patenting activities to maximize the effective patent lives of their drugs? In the second step, we view strategic in a narrower sense and assess whether those patents that appear to be strategically timed represent less innovative efforts.

### A. Strategic Timing Analysis

#### *1. Strategic Timing Analysis: Predictions*

First imagine a model in which secondary-drug innovation and associated patenting practices are not strategically timed. After a biologics manufacturer has developed and patented the primary molecule associated with their biologic, they continue to research and develop associated technologies—e.g., delivery devices, formulations, etc. Assume they approach these post-primary R&D activities with an intensity that evolves smoothly over time—e.g., as a result of a development process involving some amount of growth or decay. Moreover, considering that the U.S. resolves patent races with reference to those who file patent applications first, assume that firms will file the associated patents soon after they develop the innovation.[23] With these two assumptions, in expectation, one would predict that biologics firms will patent secondary drug features in the post-primary-filing period in a manner that likewise evolves smoothly over time.

[23] Relatedly, delaying on filing novel and nonobvious innovations until later dates runs the risk of prior art—e.g., other patents or scientific articles—emerging in the interim and invalidating the relevant patent.

Now, imagine a strategically timed alternative, whereby firms time their development and associated patenting activities to satisfy two objectives: (1) maximize the duration over which some patent covers the drug and (2) ensure that the relevant drug maintains continuity in patent protection—i.e., no or minimal temporal gaps in patent protection. It is straightforward to show that firms will meet these two objectives by developing subsequent technologies and filing associated patents prior to the expiration of the preceding patents (meeting objective 2) and as close as possible to the expiration of the preceding patents (meeting objective 1, considering that patent terms toll from filing). This would produce a temporal path of patenting activity that presents with a period of growth followed by a discrete dip.

What might drive firms to set those two objectives in the first place? Recall from Part III(C) that even though patents on specific drug features only directly block products with those features, the blocking impacts of secondary patents may spillover to impact versions of those drugs without such features. For instance, by filing a secondary drug patent, firms may ensure exclusion of entrants using the new drug features, and by doing so before the expiration of the initial patents, firms may hope to move the consumer/physician base to versions of the drug with the new features before biosimilars have an opportunity to enter and gain momentum in the market under the initial versions (Carrier and Shadowen 2016).[24]

Both the strategically- and non-strategically-timed models may result in patenting activity in the years following the primary patent and thus possibly explain the patterns depicted in Figure 3. The models differ, however, in the smoothness of the patenting practices one would expect to observe around the expiration of earlier patents. Accordingly, to mediate between these models, we test whether firms' subsequent patenting activity is concentrated prior to the expiration of the

[24] To be clear, our analysis will not directly test for evidence of product shifting/hopping, as we will only be exploring patenting practices per se, but we will nonetheless test the key role played by patents in this broader strategy (Carrier and Shadowen 2016).

preceding patents and strongest just short of that preceding-patent expiration. To get analytical traction on this prediction, we explore patenting activity in an event window surrounding the expiration of the most significant preceding patent: the primary patent covering the main molecule associated with the biologic.[25]

We acknowledge that, at the moment the primary patent expires, it may not necessarily be the last expiring patent associated with the relevant drug. Consider, for instance, a patent, Patent B, that is filed several years after the 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 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.[26]

Altogether, we predict under a strategic-timing model that biologics manufacturers will target a disproportionate share—though not necessarily the entirety—of their subsequent patent filings in the period just before the expiration of the primary patent.

### *2. Strategic Timing Analysis: Methodology and Results*

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

[25] We flag the primary patent by identifying the earliest "Main Compound" patent recorded in our database.
[26] 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.

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.

Importantly, 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.[27] We also focus on event windows in the post-2010 period. As discussed in Part IV above, Congress effectively created the biosimilar competitive threat at this time, leaving strategic evergreening motivations less relevant prior to this time.[28]

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-

[27] Continuation patent applications are new applications that allow applicants to see 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.

[28] 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.

by-time period—where time is measured with reference to the timing of patent filings relative to primary-patent expiration—and 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.[29] We begin with the simple event-study specification without control drugs:

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

where $e$ indexes the treatment-event time and $i$ the biologic. $EXPIRE_e$ represents a set of dummy variables capturing the event-time associated with the incidence of the treatment drug's primary-patent expiration. Drug fixed effects are captured by $\delta_i$.[30]

We present estimates of the $\beta_e$ 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).[31] 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):

[29] Our results are virtually unchanged when estimating Ordinary Least Squares specifications, as we show in Figure A8 of the Online Appendix.
[30] 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.
[31] 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.

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

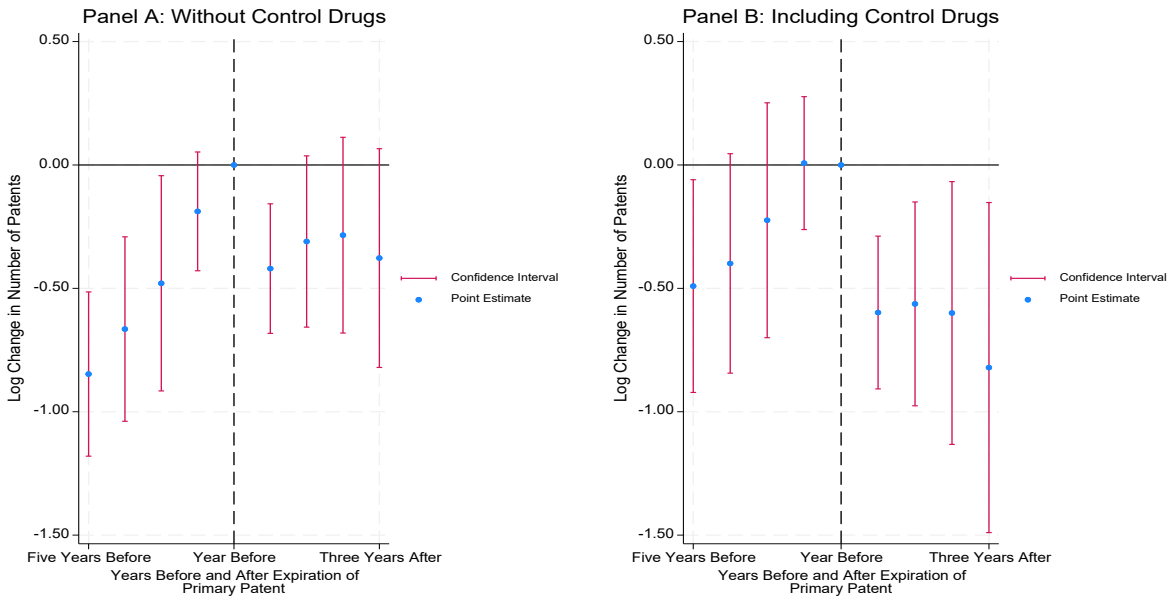
where $D_i$ is an indicator for the treatment group and other parameters are as above. Control drugs are assigned the same event-time indicators as the corresponding treatment drugs within the relevant layer of the stack.[32] The coefficients of the interactions between these event-time indicators and an indicator for the treatment drug—i.e., the $\beta_{2e}$ coefficients--represent the objects of interest. This specification is intuitive and essentially estimates a 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.[33]

In Panel B of Figure 4, we present the estimated $\beta_{2e}$ 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 patenting once the primary patent expires.[34] Moreover, the magnitudes of these swings are considerable, with the Poisson regression

[32] Results are identical if event dummies are included, as events are perfectly identified by drug dummies and treatment status.
[33] 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.
[34] 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.

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.

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.

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 model, the timing of the relevant jumps we document align precisely with the incentivized moment in time under the strategic model.

### *3. 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.

In Table A1 and Figure A11 of the Online Appendix, we also estimate these behaviors by patent type. Consistent with the preliminary evergreening evidence from Part V, we find the strongest evidence of strategic evergreening 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. Accordingly, these heterogeneous findings lend confidence to an interpretation of the evergreening findings depicted thus far as being strategic in nature.

Finally, 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 VII below).

## B. Innovativeness of Strategically Timed Patents

### *1. Innovativeness Analysis: Overview*

Even if the strategically-timed secondary patents depicted in Figure 4 represent true innovations—i.e., are novel, nonobvious leaps over the prior art—the behavior depicted may still be strategic in the sense defined in the Introduction. The timing patterns are consistent with a

motive that entails excluding competition bearing on the brand/drug in its entirety, not just versions of the drug with the relevant features. That being said, it is possible that this evergreening behavior may depart even further from the traditional justification for patents should those strategically timed secondary patents also be non-innovative in nature. Under this possibility, manufacturers may be 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 latter 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, 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 shed light 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 or rejected.

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 determination, 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]

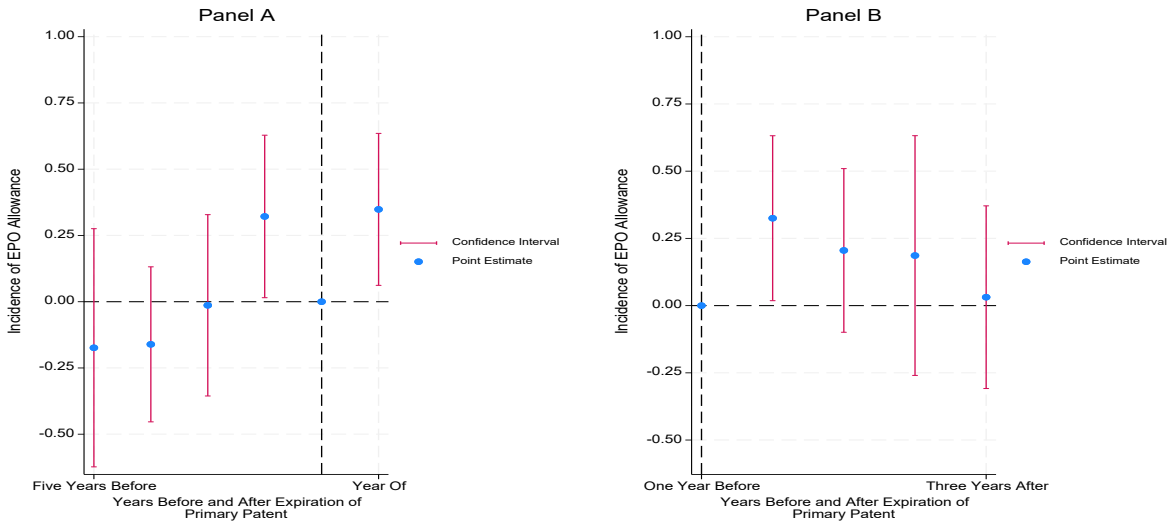
Focusing first on Panel A of Figure 5, we find that indicators of innovativeness among filed biologics patents increase as the patent expiration of the drug's primary patent nears. However, in the year before that expiration, there is a precipitous drop in the innovativeness indicator. As both Panel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

[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).

allowance rate once the primary patent expires. The elevated innovativeness of those patents filed the year of expiration may be a spillover 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.

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.

Interestingly, these findings are consistent with *both* the non-innovative gaming story and its alternative where firms are strategically timing seemingly 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.

### *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. Moreover, we find suggestive evidence that some of those secondary patents filed for such purposes are of more questionable legal validity.

## VII. Relationship between Patenting and Biosimilar Entry/Threat

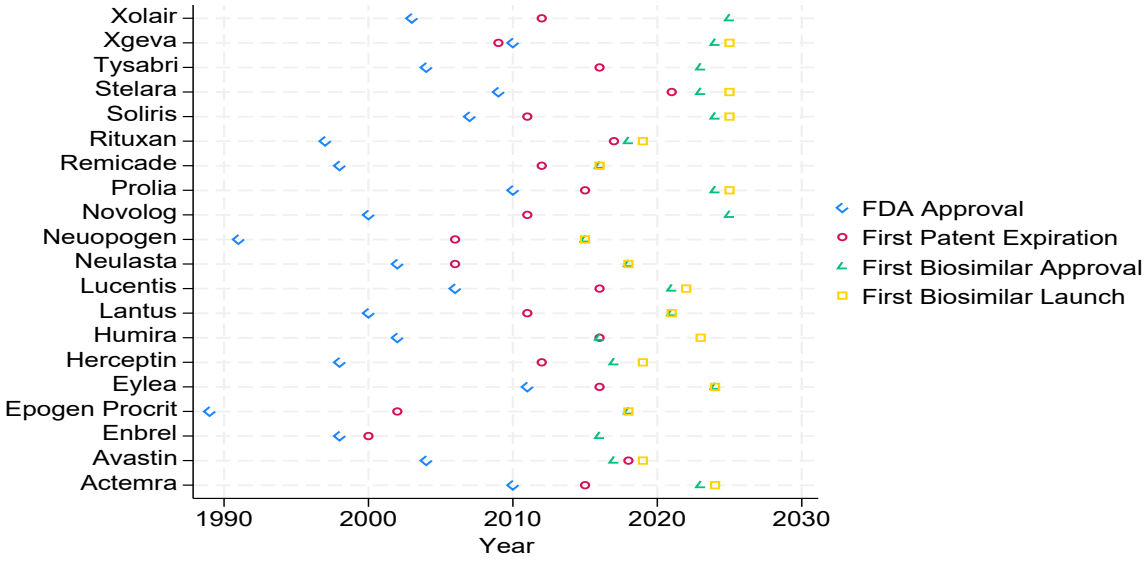
The evidence of thicketing and evergreening set forth above demonstrates the potential for biologics patent portfolios to meaningfully forestall competition from biosimilars. In this Part, we discuss whether this potential, in fact, materializes. Primarily, we consider several descriptive observations 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]

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.

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 roughly 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 others such as Enbrel will be waiting an additional set of years before biosimilar launch. Notably, the effective market life of a given

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

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 (Hemphill and Sampat 2025).

It may be premature, however, to draw meaningful 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.

## VIII. 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),

[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.

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.

The welfare implications of our above findings—in addition to the simulated impacts of the APPA—are rather nuanced. As discussed in Part VI, 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 VI do suggest that some of those strategically timed secondary drug patents represent novel, and non-obvious innovations—e.g., imagine a new injection mechanism that decreases administration discomfort and that improves drug adherence.

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. That is, welfare harms may arise from the fact that the relevant decisionmakers over whether to use the new drug versions are not assessing whether the benefits of using versions of the drugs with the new, innovative features are nonetheless worth the marginally higher prices. While the Patent Office does an innovativeness screen, that screen is not designed to track this cost-benefit analysis (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

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

the APPA and 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).

## IX. 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 (Budish et al. 2015). 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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[40] Relevant studies include Acemoglu and Linn (2004); Blume-Kohout and Sood (2013); Dubois et al. (2015); Gilchrist (2016); Rake (2017); Myers and Pauly (2019); Dranove et al. (2020); and Chen et al. (2025).

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Online Appendix to:

# STRATEGIC PATENTING: EVIDENCE FROM THE BIOPHARMACEUTICAL INDUSTRY

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Preliminary Note: additional legal details regarding the biologics and small-molecule regulatory structures and the Affordable Prescriptions for Patients Act can be found in Frakes and Wasserman (2025), which is a working paper prepared for a law review. This law-review counterpart also offers certain additional details regarding the science of biologics as it relates to the choices made in constructing our novel biologics patent database. In other words, this law-review working paper is meant to supplement the present Online Appendix to provide additional background for the present article.

Frakes, Michael, and Melissa Wasserman. 2025. "Unveiling the Patent Landscape of Biologic Drugs," unpublished working paper.

## Reasons for Lack of Comprehensiveness of Purple Book

For two key reasons, the comprehensiveness of the disclosures associated with the Purple Book falls far short of that associated with the Orange Book. First, biologics patent disclosures are produced though a complicated sequence of negotiations between the brand and biosimilar known as "the patent dance," but this process is itself only voluntary. Second, the original biologic firm does not need to disclose all the patents that cover its product, as is required in the small-molecule regime, but instead only those that it believes will be infringed by the *specific* biosimilar with which it is engaged in the "patent dance." It is possible that the originating firm might assert a different set of patents against another biosimilar.

## Discussion of Construction of Database and Orbit Intelligence Search Process

The following language is drawn largely from Frakes and Wasserman (2025), which, as above, provides greater scientific and legal detail surrounding the construction of the biologics patent database.

The methodology and resources used to build the patent landscape for each drug included the following steps: (1) identifying patents listed on the Purple Book, (2) where

applicable and publicly available, identifying patents asserted in litigation in the United States in relation to the biologic, (3) where applicable and publicly available, identifying patents asserted in Patent Trial and Appeal Board (PTAB) proceedings in relation to the biologic, (4) identifying patents that received a patent term extension under 35 U.S.C. §156, which is designed to restore patent term lost during the FDA's review process and (5) conducting patent searches utilizing Orbit Intelligence patent analytic and search software.[41] Any patent that was listed in the Purple Book or asserted in federal litigation or in a PTAB proceeding was automatically included in the patent database. However, we took a different approach with the patent searches as more care and time is required to identify patents that possibly meet our inclusion criteria and to validate which patents meet these criteria.

To avoid the risk of otherwise misapplying our inclusion criteria through an attempt to automate the detection of these kinds of failures, we read and hand-code all patents that were identified utilizing our search methodology before including them in our database. 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 our search protocol in different stages, across which we trade off different search parameters.

Our initial search of all patent types focused on identifying relevant patents owned by the corporate entity that filed the license for the biologic and any additional corporate entity were there was significant evidence of involvement in the development, marketing, or ownership/licensing history of the biologic.[42] This initial search includes keywords related to the biologic, including the Trade name (i.e. Humira), the chemical name (i.e. adalimumab), the internal identification code of the biologic (D2E7), and the drug class of the biologic (i.e. Tumor Necrosis Factor). These keywords were cross referenced using Orbit Intelligence with the title, abstract, and claims of the patent documents. If no results were returned within the corporate tree, then the search was expanded to also include matches within the full text of the patent document. In some cases, the text of a document made clear that it read on a particular biologic, but the claims only referenced to "drug" or some other general term. We only include a patent if the claims indicated the biologic in question was the subject of the claim.

An additional initial search was conducted for patents related to delivery of biologic drugs through approved delivery methods (infusion, injection, etc.)—i.e., device patents—only. This additional search focused on the same corporate entities and the same keywords as the initial search. However, this additional search for device patents was broader in one aspect and narrower in another aspect than the initial search. It was narrower in that it required the word "device" or other delivery methods related to the biologic (i.e., inhaler, etc.) to be in the claims of the patent document. The additional search of device patents was

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[41] One benefit of Orbit Intelligence software is that it allows for the easy grouping of assignees of patents based on the responsible corporate entity—i.e., the entity that filed the biologics license application, including all subsidiaries that may have a different name. For example, searches for biologics owned by Johnson & Johnson would include results for Janssen Pharmaceuticals, Centocor, and Acelion among others. Including all corporate entities with direct ties to the responsible marketing party gives the highest likelihood of finding relevant publications.

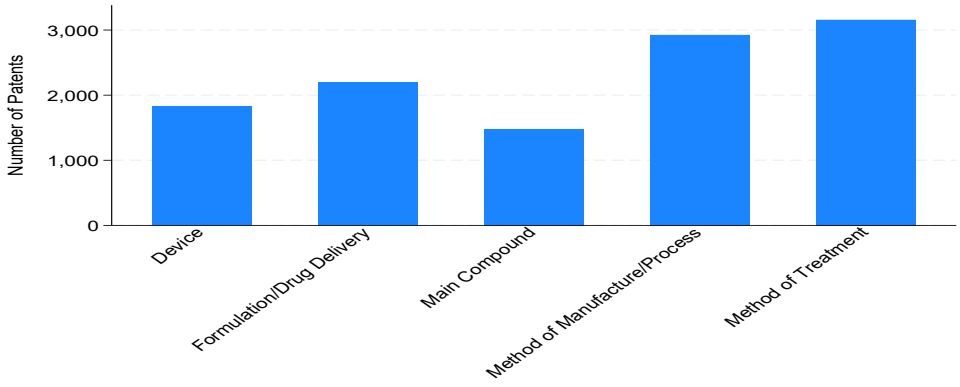
[42] Additional parties are sometimes involved in the development, marketing, or ownership of a biologic that are not the reference product sponsor. These additional entities were identified by either a general internet search, the use of Adisinsight database by Springer, or the use of LexisNexis database.

broader than the initial search in that the keywords (i.e., Trade name, the chemical name, the internal identification code of the biologic, and the drug class of the biologic) were not limited to matches within the title, abstract, and claims of the patent documents but instead within the full text of the patent document.

The second patent search of all patent types was broader in one aspect and narrower in another aspect than the initial search. The second patent search did not restrict the patent search to be within the corporate entities that either filed the license and/or were involved in the development, marketing or ownership of the biologic. However, the second search was narrower in that it did not include keywords related to the drug class of the biologic (i.e., Tumor Necrosis Factor), as doing so returned far too many non-relevant results. That is, the keywords in our second search included those related to the Trade name (i.e., Humira), the chemical name (i.e., adalimumab), and internal identification code of the biologic (D2E7), which were cross-referenced using Orbit Intelligence with title, abstract, and claims of the patent documents. Importantly, for this second stage, we searched patents assigned to any assignee, not just those that are part of the corporate entity that filed the biologic license.

Finally, we conducted a third search of all patent types using biosequences (nucleotides or amino acids) for the FDA-approved biologic to find any results where the biologic was only referred to in the claims of the patent as a numbered sequence rather than by its chemical name, trade name, or internal identifier. Sequences were obtained from Drugbank Online or Kegg Drug in most instances. If sequences could not be found in those two sources, then previously found publications were searched for reported sequences that were designated as matching that of the biologic by name. Patent documents were searched for inclusion of the matching sequence within the claims section of the document. A matching sequence was determined to be either a full sequence match to the reported sequence or one that comprised part of the sequence. Some genetic mutations were included if there was enough other evidence to indicate that the mutant in question was indeed a variant of the indicated biologic and the mutant had a greater than 95% match with the reported sequence of the biologic.

Figure A1. Number of Patents by Patent Type, Across Sample of Drug/Patent Pairs




Note: data are from 11,595 patent/drug pairs associated with 515 biologics approved by the FDA.

Every patent was assigned to only one type of patent. Those types are defined as follows:

(1) *Main Compound*: A patent that claims a biological compound, including a specific amino acid sequence,[43] a specific conjugate,[44] or a specific post-translational modification to a protein or antibody.

(2) *Method of Treatment*: A patent that claims the use of a biologic to treat an indication or group of indications.[45] Method of treatment patents were included in our database only if the biologic was FDA-approved for the claimed indication.

(3) *Method of Manufacturing*: A patent that claims a process utilized to manufacture a biologic,[46] including methods to chromatographically separate the biologic, methods to culture the biologic, or other methods involved in the biological manufacture process.[47]

(4) *Formulation*: A patent that claims the way a biologic is formulated and/or administered, including routes of administration, dosages, formulations including non-active additives,[48] non-conjugated drug carriers, and extended-release, etc.

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43 *See, e.g.*, U.S. PAT. APP. NO. 2017/0349665 (filed June 16, 2017), which claims a specific anti-human-CD52 antibody comprises an amino acid sequence, is an example of a patent that claims a specific amino acid.

44 *See, e.g.*, U.S. PAT. APP. NO. 14/721,761 (filed May 26, 2015), which claims a conjugate between a water-soluble polymer and a peptide, is an example of a patent that claims a conjugate.

45 *See, e.g.*, U.S. PAT. NO. 11,116,808 (issued Sept. 14, 2021), which claims the use of Candida albicans for the treatment of wards, is an example of a patent that claims a method of treatment.

46 *See, e.g.*, U.S. PAT. APP. NO. 16/840,293 (filed Apr. 3, 2020), which claims the manufacturer of a drug product with parameters on the glycoprotein composition.

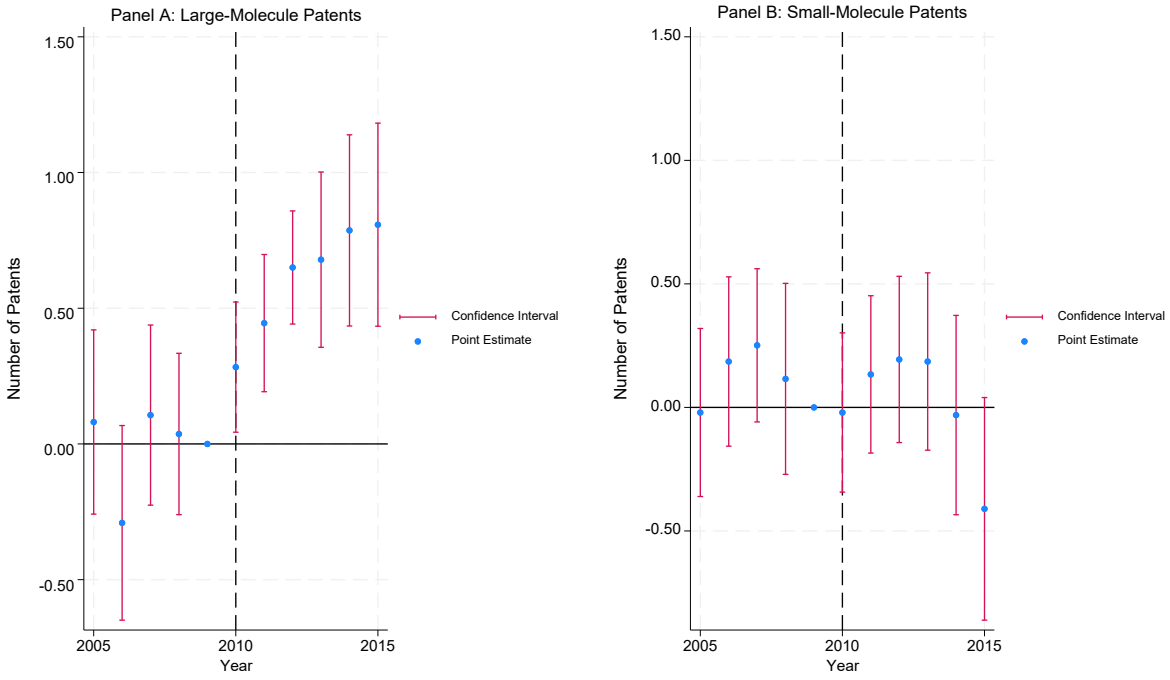
47 *See, e.g.*, U.S. PAT. NO. 6,381,336 (issued Apr. 30, 2002), which claims a process for purifying an immunoglobulin from a crude mixture.

48 *See, e.g.*, U.S. PAT. NO. 9,241,897 (issued Jan. 26, 2016), which claims the preparation of an immunoglobin with an added concentration of proline to adjust the viscosity of the preparation.

(5) *Device*: A patent that claims a specific device used in the administration or preparation of a biologic, including kits, injection devices,[49] or other such objects.

BPCIA-Enactment Analysis: Robustness

Figure A2. 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 (Poisson Specifications)




Notes: this figure replicates the analysis from Figure 1 except estimating Poisson specifications.

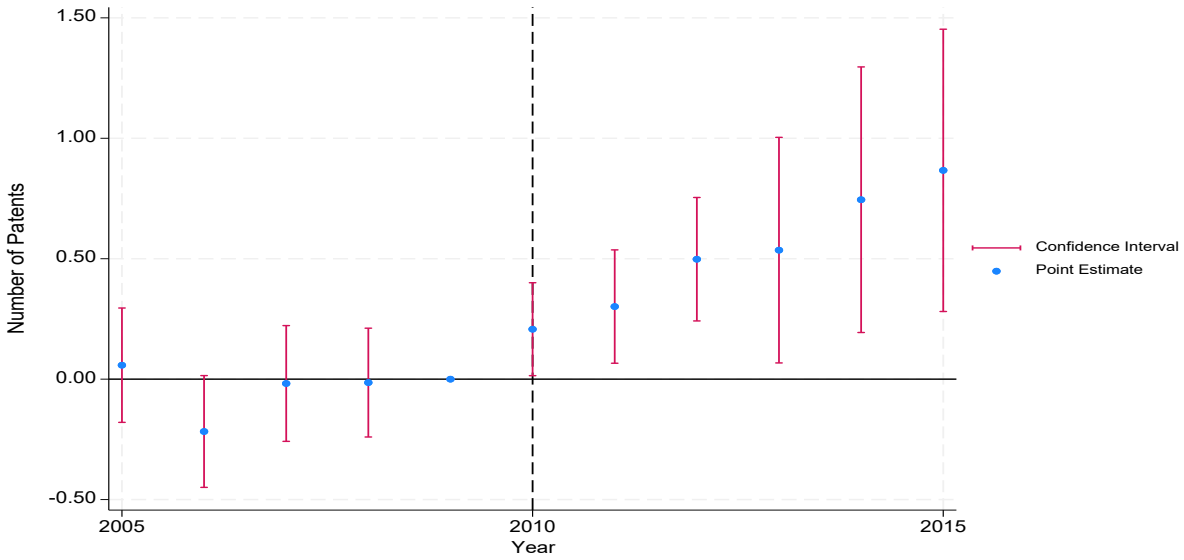
49 *See, e.g.*, U.S. Pat. No. 11,806,507 (issued Nov. 7, 2023), which claims an infusion device for the administration of the biologic.

We now formalize the comparison of the large and small molecule response to the BPCIA in Figure 1 of the text. Specifically, we pool the large and small molecule samples of drug-by-year pairs and estimate the following difference-in-differences specification:

(A1)
$$Patent\_Count_{it} = \alpha + \boldsymbol{\delta_i} + \beta_1 LARGE_i + \sum_{\boldsymbol{t=2005}}^{\boldsymbol{2015}} \beta_t YEAR_t + \sum_{t=2005}^{2015} \beta_{2t} LARGE_i \; X \; YEAR_t + \varepsilon_{it}$$

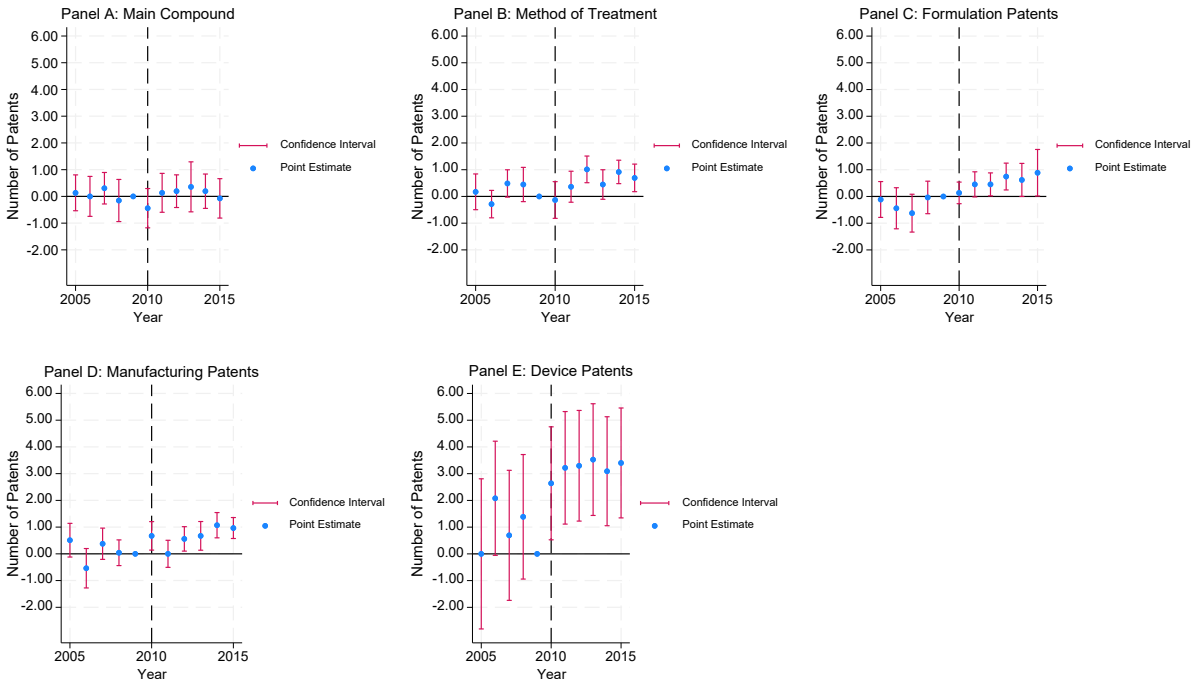
We then present the estimated $B_{2t}$ coefficients in Figure A3.

Figure A3. Estimated Differential Patenting Response to the BPCIA Enactment between Large and Small Molecule Drugs (Among Drugs Approved by 2009): Event-Study Results



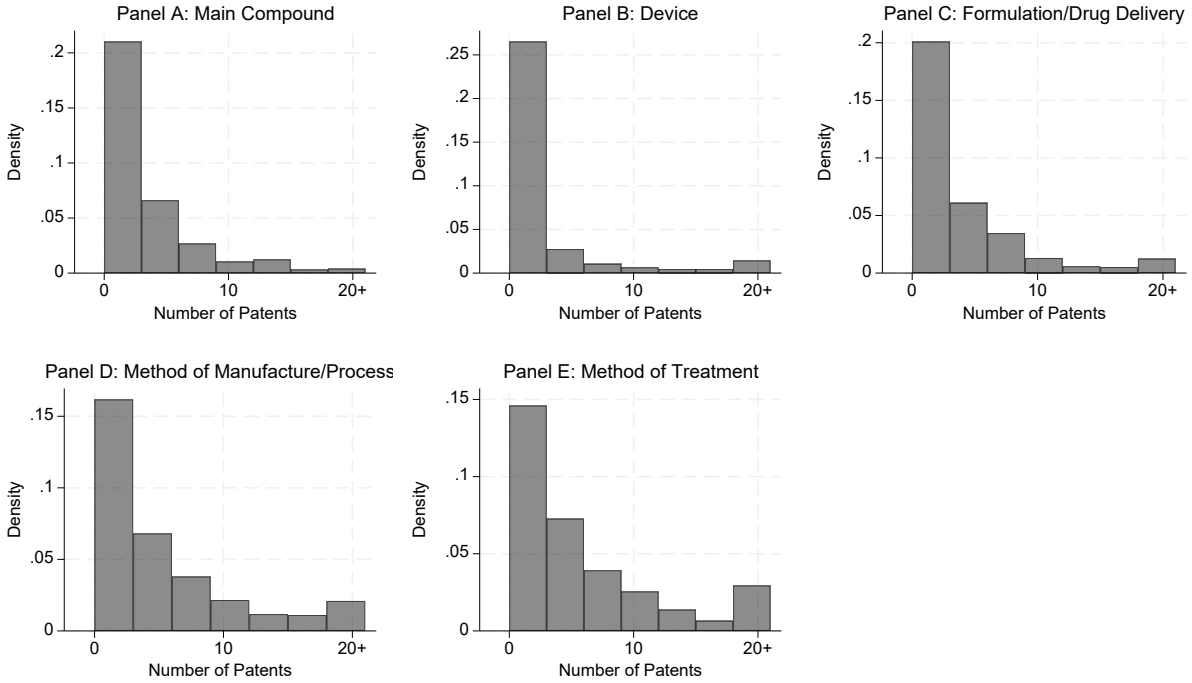

Notes: this figure presents results from specification A(1), specifically plotting the estimated $B_{2t}$ coefficients.

Figure A4. Patenting Activity in Years Leading up to and Following BPCIA for Large-Molecule Drugs (Approved by 2009), Separately by Patent Type



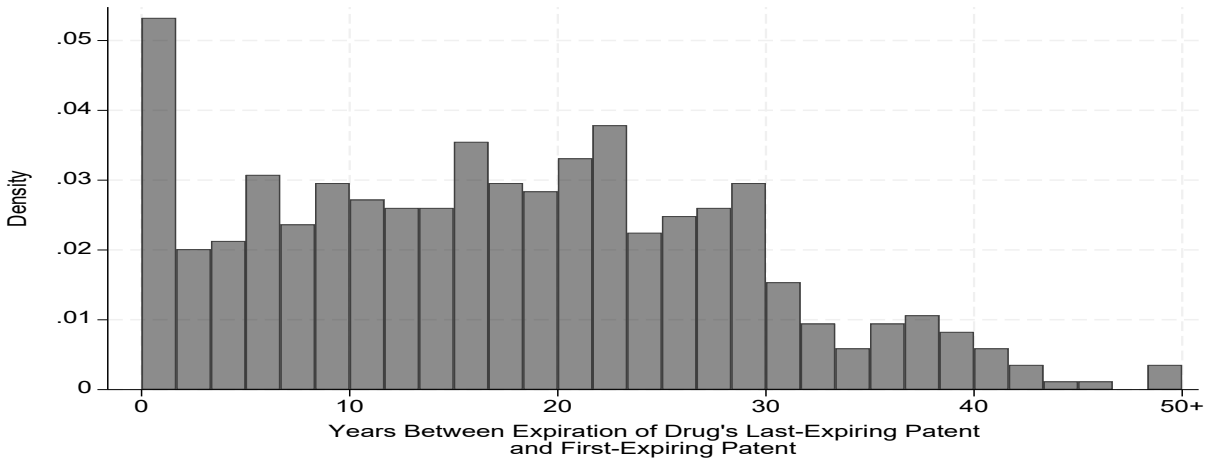

Notes: this analysis replicates that of Panel A of Figure 1, separately by patent type.

Figure A5. Histogram of Patents-Per-Drug across Large-Molecule Drugs, Separately by Patent Type



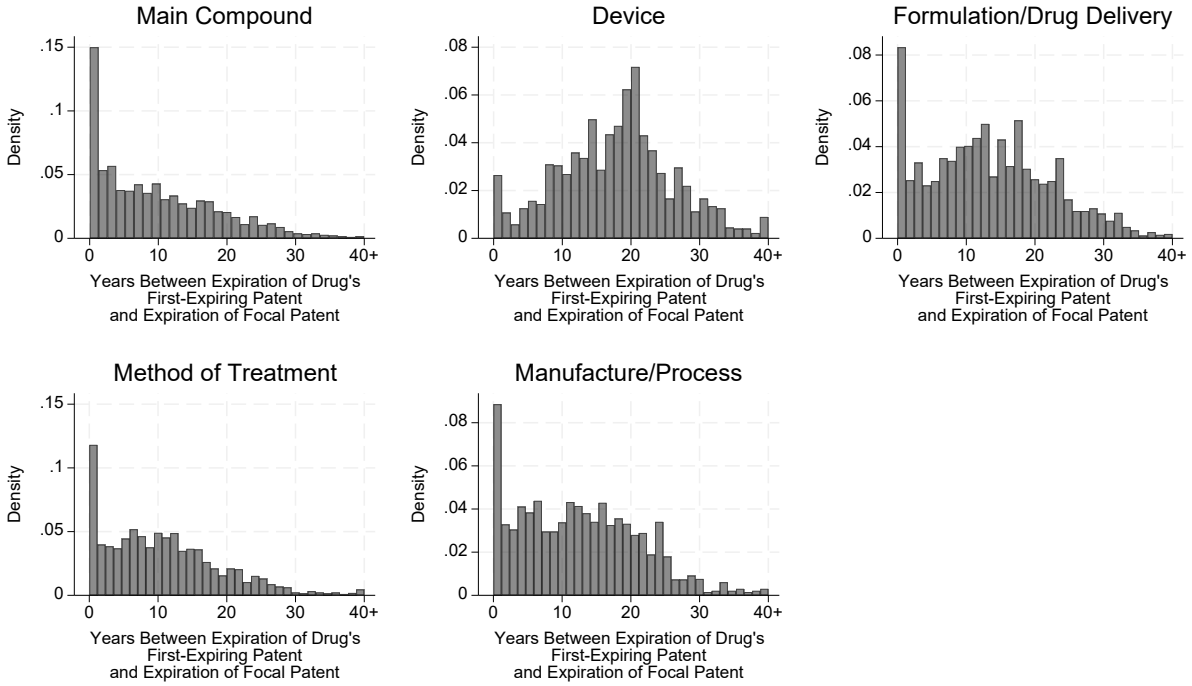

Note: data are from a sample of 515 biologics approved by the FDA.

Figure A6: Histogram of Difference in Years Between First- and Last-Expiring Patent Per Drug



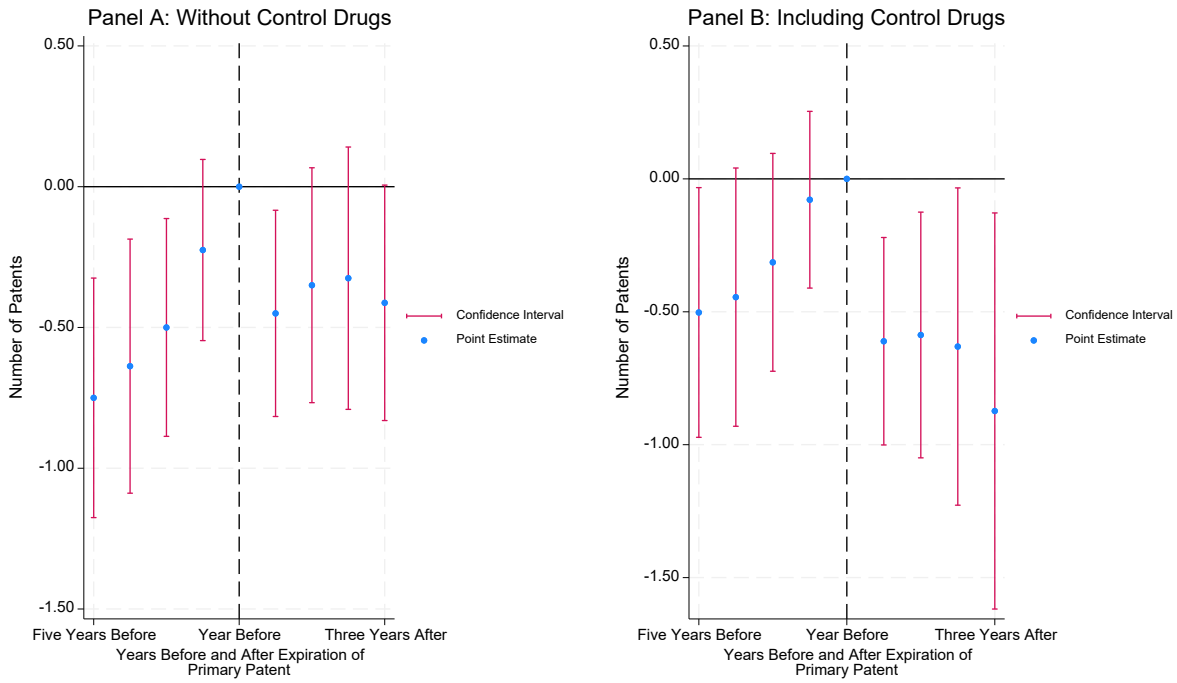

Note: data are from a sample of 509 biologics approved by the FDA with at least one patent.

Figure A7: Histogram of Difference in Years Between Drug's First-Expiring Patent and Focal Patent, by Patent Type (Among Sample of Drug-Patent Pairs)




Notes: data are from a sample of 15,595 drug-patent pairs.

Figure A8: Patenting Activity in Years Leading up to and Following Primary Patent Expiration: Ordinary Least Squares Event-Study Specification Results




Notes: this figure replicates that of Figure 4 in the text, but instead estimating Ordinary Least Squares specifications.

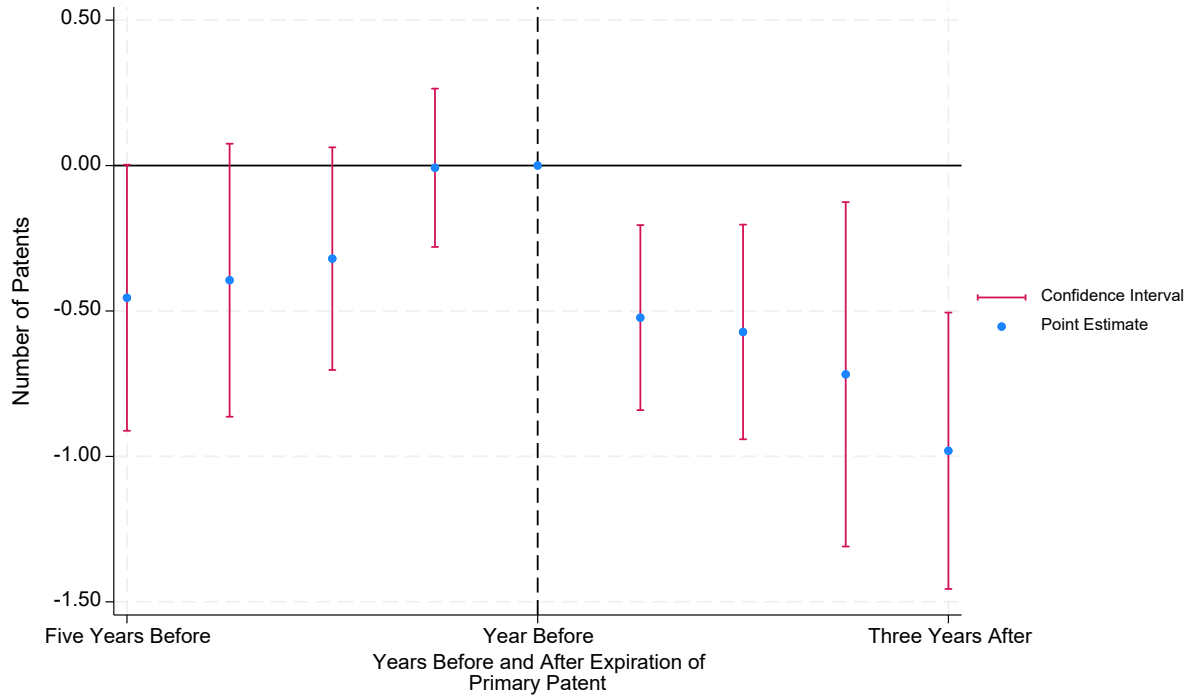
Cengiz et al. (2019) Version of Event-Study Specification

We next estimate the following specification:

$$Patent\_Count_{eit} = \exp\left(\alpha + \boldsymbol{\partial_{et}} + \boldsymbol{\delta_{ei}} + \sum_{\boldsymbol{e=-4}}^{\boldsymbol{4}} \beta_e EXPIRE_e + \varepsilon_{eit}\right)$$

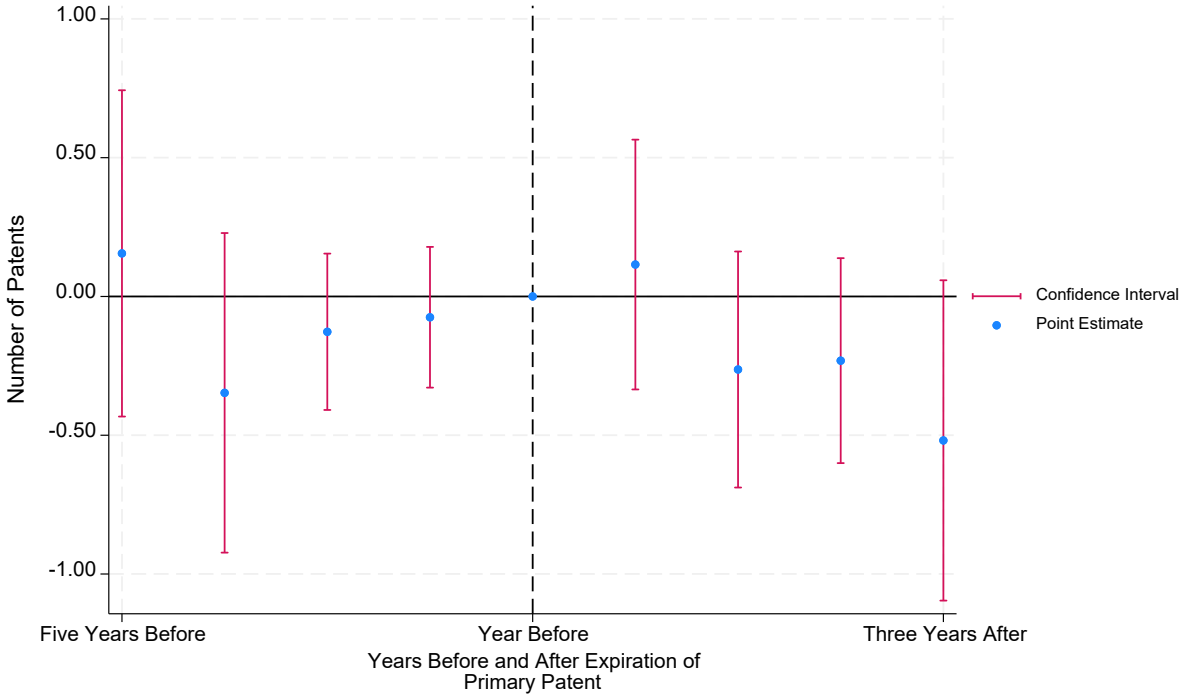
Where $\boldsymbol{\partial_{et}}$ and $\boldsymbol{\delta_{ei}}$ represent event-by-calendar-time fixed effects and event-by-drug fixed effects. Now, unlike with the Wing et al. (2024) specification estimated in the text, the event-time indicators, EXPIRE, are turned on for the treatment drugs only.

Figure A9: Patenting Activity in Years Leading up to and Following Primary Patent Expiration (with Control Drugs): Cengiz et al. Specification




Notes: this figure shows results from an analysis replicating that of Panel B of Figure 4 but instead estimating the Cengiz et al. (2019) specification.

Figure A10. Falsification Exercise: Continuation Patenting Activity in Years Leading up to and Following Primary Patent Expiration.




Notes: this figure replicates the analysis from Panel B of Figure 4 but focusing on the frequency of patenting of continuation applications, based on the date in which continuations are filed.

Patenting Around Primary Patent Expiration: By Patent Type

By breaking the analysis up by patent type, we add additional noise to the estimation exercise. To improve, we focus on a simpler question: is the level of patenting greater before the expiration of the primary patent relative to after, within the relevant event window. That is, to get more power, we retreat from estimating year-by-year parameters and instead estimate a binary before-after parameter. Based on the predictions from Part VI, we predict that patenting will be higher pre-primary-expiration due to the objective of patenting prior to the primary expiration. For these purposes we estimate a version of the Wing et al. (2024) specification underlying Figure 4 that includes only a single before-after event indicator rather than a series of event-year dummies.

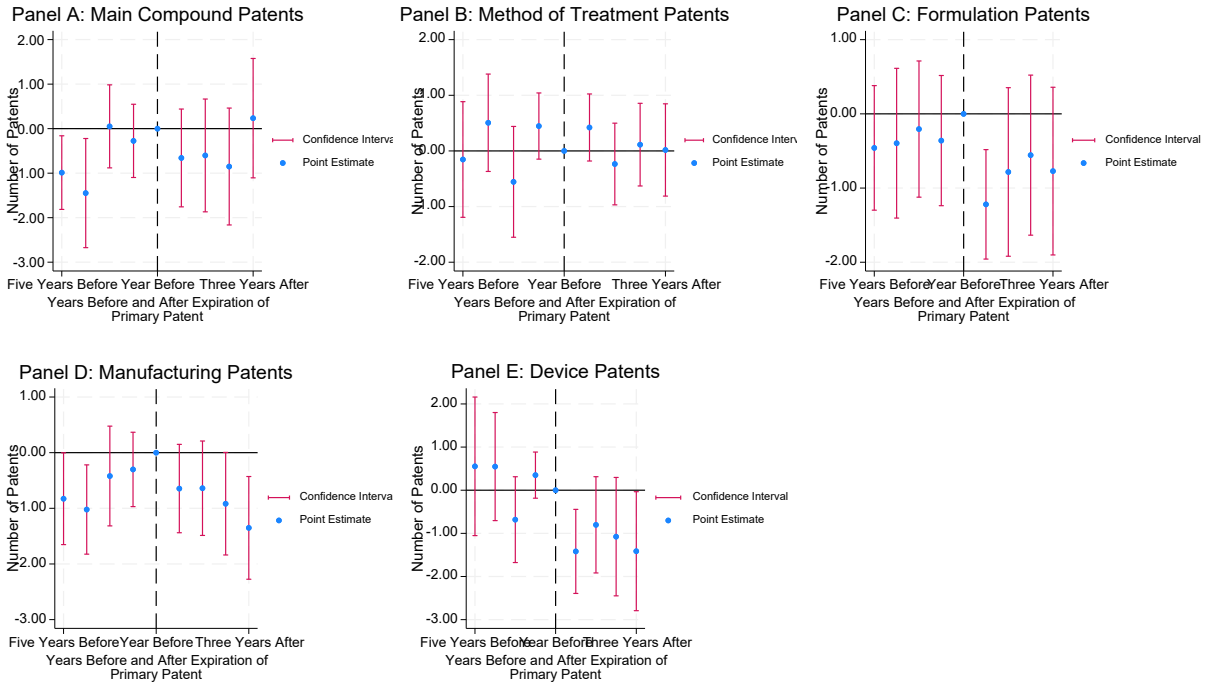
Table A1. Change in Patenting Frequency After Primary Patent Expiration by Patent Type

| | Main Compound | Device | Formulation/Drug Delivery | Method of Treatment | Method of Manufacturing / Process |
|---|---|---|---|---|---|
| Treatment X Post-Primary Expiration | 0.060 | -1.308*** | -0.543* | -0.005 | -0.422* |
| | (0.345) | (0.480) | (0.308) | (0.246) | (0.242) |
| N | 3429 | 3429 | 3429 | 3429 | 3429 |

Notes: this table presents results from specifications analogous to those estimated in Panel B of Figure 4, except that instead of estimating event-year dummies (and their interactions with treatment drug indications), we estimate a binary indicate for falling in the post-primary-expiration period. Moreover, we estimate these specifications separately by patent type, with the reported coefficient representing the log change in the number of patents filed after the primary expiration relative to before, for treatment drugs relative to control drugs. *** represents significance at the .01 level, ** at the .05 level and * at the .1 level.

Even though the year-by-year analysis is noisy, we nonetheless still show the year-by-year version—i.e., the counterpart to Panel B of Figure 4 by patent type, to evaluate whether these falls in patent frequency predate the primary-patent expiration (which would otherwise challenge a causal interpretation). We show these results in Figure A11. If anything, as expected, we estimate a general rise in patenting frequency pre-primary-expiration (except for device patents, where the pre-expiration level remains flat, but nonetheless notably higher than the post-expiration level).

Figure A11: Patenting Frequency in Years Leading up to and Following Primary Patent Expiration, by Patent Type




Notes: this analysis replicates Panel B of Figure 4, but separately by patent type.

Event-Study Analysis and Treatment of Expiration of FDA Exclusivity

Our primary analysis of strategic evergreening practices explores bunching of patenting activity in the period prior to the expiration of the legally strongest prior patent—i.e., the primary molecule patent. Our evidence suggests that manufacturers may be strategically timing their patenting activity so as to maximize the length of patent protection covering the drug.

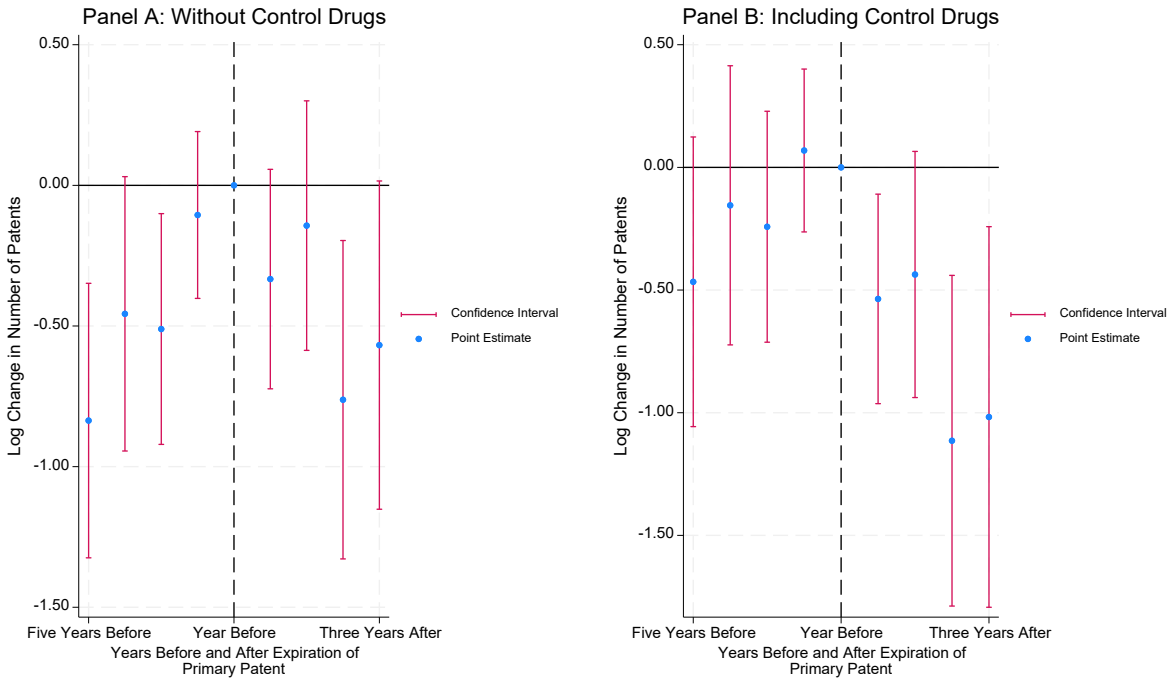
There is another significant source of exclusivity facing biologics other than patent protection. Pursuant to the BPCIA, biologics, upon FDA approval, are given 12 years of market exclusivity, over which time the FDA will effectively preclude biosimilars from entering the market (for those biologics that received FDA approval prior to the BPCIA, 12 years was still calculated from the date of their FDA approval). In this section of the Online Appendix, we also consider the possibility that firms strategically time their patenting activity to fall just before the end of this 12-year FDA-imposed exclusivity period.

We actually begin this exercise by revisiting our analysis of strategic timing around the expiration of the biologic's primary patent—Figure 4 of the text—but estimating that analysis on a sample of drugs that does not experience a loss of FDA exclusivity during the sample window. Doing so, we drop 22 out of the 80 treatment drugs explored in Figure 4. We show the results from this new exercise in Figure A12. Perhaps not surprisingly given the reduction in sample size, the findings are noisier than in Figure 4; however, we estimate essentially the same pattern. Accordingly, the analysis from the text is not likely attributable to the loss of FDA exclusivity that happens to far near the end of the patent term for the primary patent.

Next, we estimate a variant of Figure 4 that uses the loss of FDA exclusivity as the relevant event. Consistent with the analysis just run, we drop drugs that experience a loss of primary-patent protection during the event window.[50] The results are somewhat noisier in this case relative to the primary-patent-expiration analysis; moreover, we document no discernable independent effect of FDA-exclusivity expiration on the timing of patenting activity.

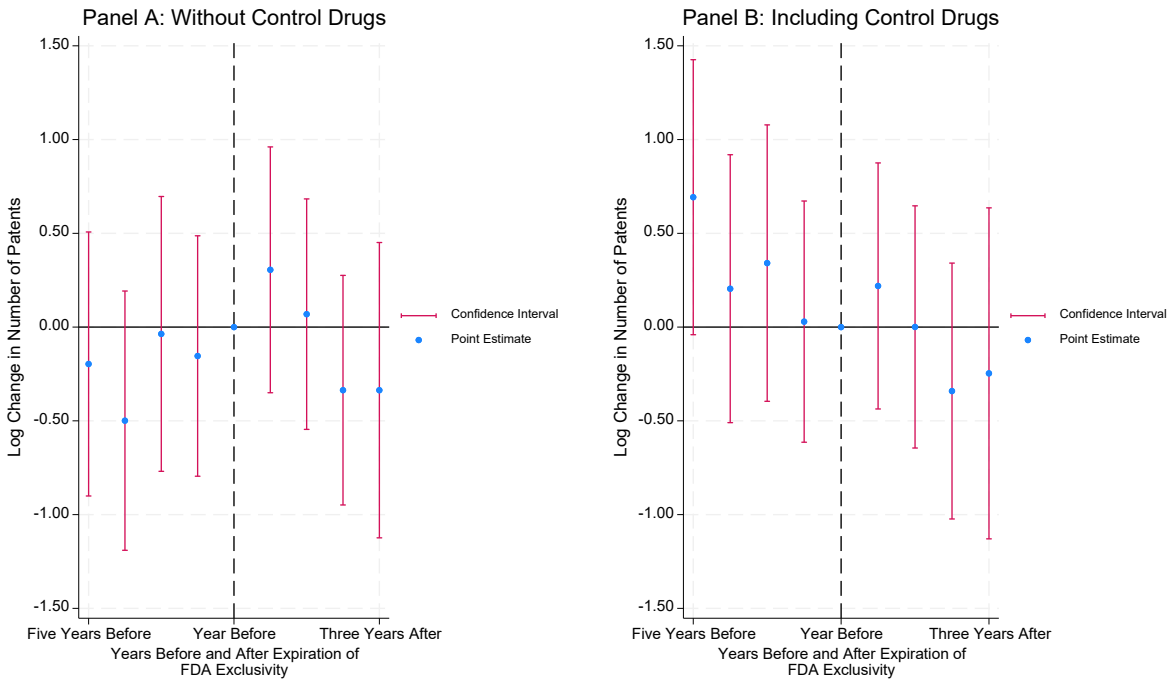
[50] With this FDA exclusivity analysis, we slightly modify the construction of the control drugs. With the primary-patent-expiration analysis, recall that for the 2015 expiration cohort, we used control drugs with primary patents that expired between 2027 and 2030. Given twenty-year patent terms, these control drugs had ostensibly begun their patenting process by the beginning of the 2015 cohort's estimation window (i.e., 2010), but would experience their own primary expirations far enough in the future that we are not likely picking up the effects of their own expiration events (including anticipatory bunching) when using them as controls. Now consider basing the "events" around the loss of FDA exclusivity. And consider the 2015 treatment cohort. If we were to use control drugs with FDA exclusivity losses between 2027 and 2030, this would entail focusing on control drugs that were approved by the FDA between 2015 and 2018. Some of those drugs approved at the end of this range did not start their patenting process by the beginning of the 2015 estimation window—i.e., 2010. Considering that we are using control drugs to help account for calendar year patenting trends, this is undesirable. Accordingly, for the purposes of this alternative FDA-exclusivity analysis, we slightly shorten the period of time we look to the future to select the control drugs. Specifically, for each treatment cohort, we select control drugs experiencing their own FDA-exclusivity-loss events between 8 to 12 years in the future (e.g., for the 2015 treatment cohort, we use control drugs experiencing exclusivity loss between 2023 and 2026). We note, however, that the conclusions from this exercise are not sensitive to this choice and are robust to using the same temporal construction of control drugs as that used in the primary patent-expiration analysis. In this vein, we also show results with no control drugs whatsoever.

Figure A12: Patenting Frequency in Years Leading up to and Following Primary Patent Expiration, Dropping Drugs with Loss of FDA Exclusivity in the Treatment Window




Notes: this analysis replicates that of Figure 4 but drops drugs with loss of FDA exclusivity in treatment window. The number of observations equals 522 in Panel A (58 treatment drugs) and 2934 in Panel B.

Figure A13: Patenting Frequency in Years Leading up to and Following Loss of FDA Exclusivity (Excluding Drugs Experiencing Expiration of Primary Patent in Treatment Window)




Notes: this analysis replicates that of Figure A12 but instead focusing the treatment event on the loss of FDA exclusivity.

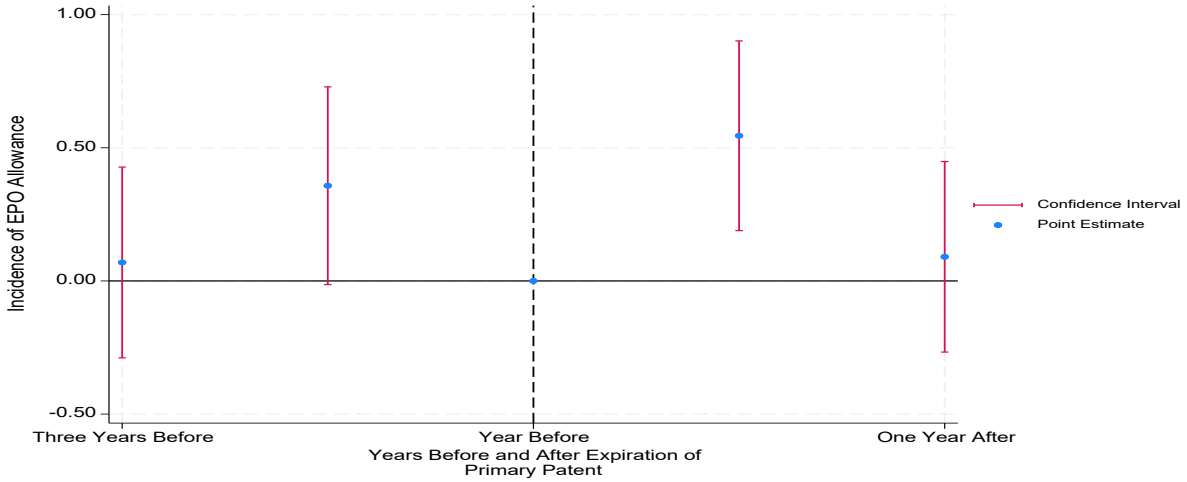
Table A2: Incidence of Allowance at EPO by US Application Year

| USPTO Application Year | Incidence of Allowance at EPO Among those also filed with EPO (N) |
|---|---|
| 2009 | 0.94 (N=200) |
| 2010 | 0.87 (N=248) |
| 2011 | 0.92 (N=318) |
| 2012 | 0.85 (N=334) |
| 2013 | 0.82 (N=312) |
| 2014 | 0.82 (N=408) |
| 2015 | 0.78 (N=400) |
| 2016 | 0.80 (N=404) |
| 2017 | 0.68 (N=488) |
| 2018 | 0.49 (N=608) |
| 2019 | 0.41 (N=530) |
| 2020 | 0.33 (N=744) |
| 2021 | 0.28 (N=742) |
| 2022 | 0.43 (N=535) |
| 2023 | 0.42 (N=219) |

Notes: data are from those biologic patent-drug pairs that are also associated with filings at the EPO.

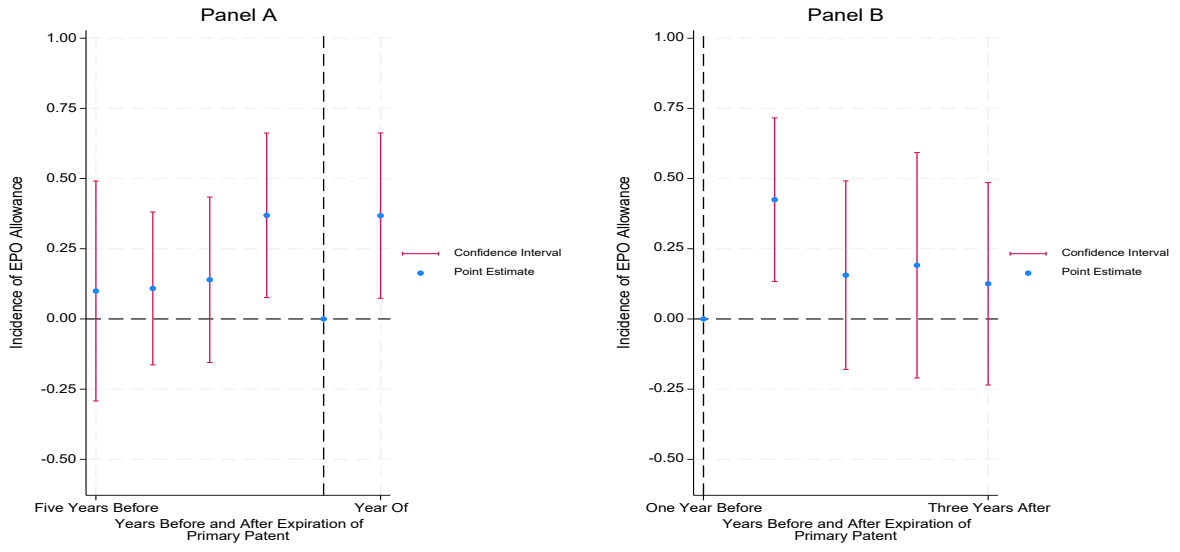
Robustness of EPO Event-Study Analysis

Figure A14: Incidence of EPO Allowance Among US Biologic Patents Filed in Years Leading up to and Following Primary-Patent Expiration (Two-Year Event Window)



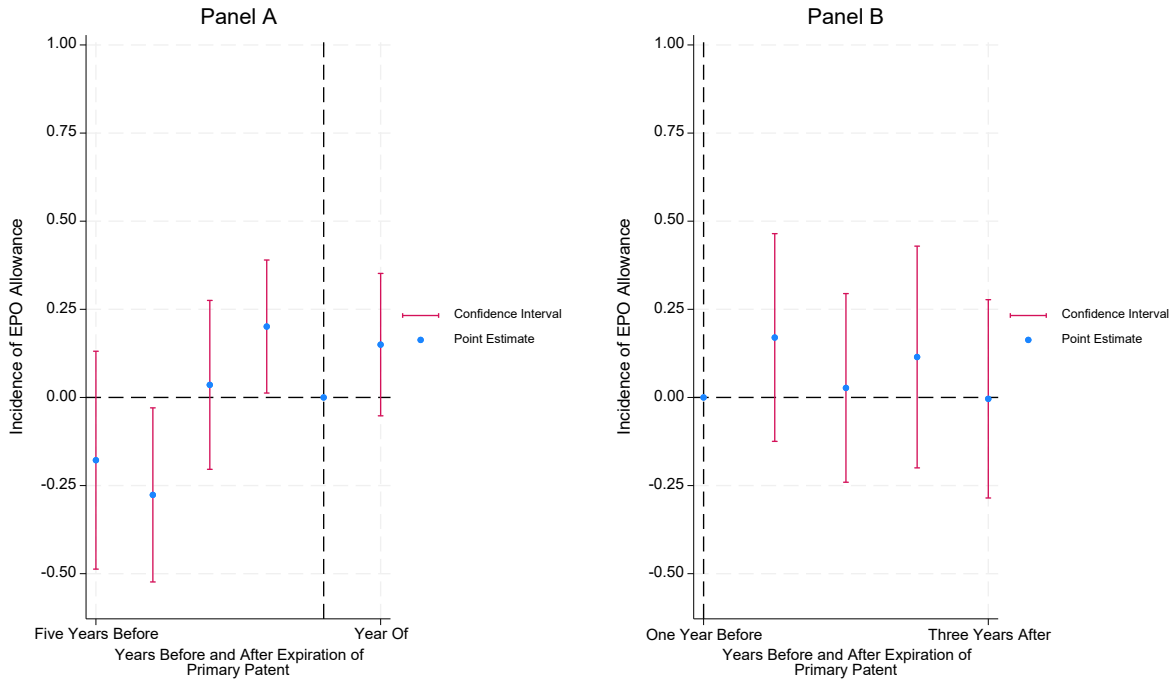

Notes: this analysis presents results from a version of specification (3) that focuses on a two-year event-window and that uses as the dependent variable the incidence of the U.S. patent application also being allowed at the EPO (among a sample of applications also filed at the EPO). N = 203.

Figure A15: Incidence of EPO Allowance Among US Biologic Patents Filed in Years Leading up to and Following Primary-Patent Expiration, Including Pre-2010 Treatment Events




Notes: this analysis replicates that of Figure 5 in the text but also including pre-2010 treatment events. N = 1111 in Panel A and 841 in Panel B.

Figure A16: Incidence of EPO Allowance Among US Biologic Patents Filed in Years Leading up to and Following Primary-Patent Expiration, Including Applications Filed through 2021

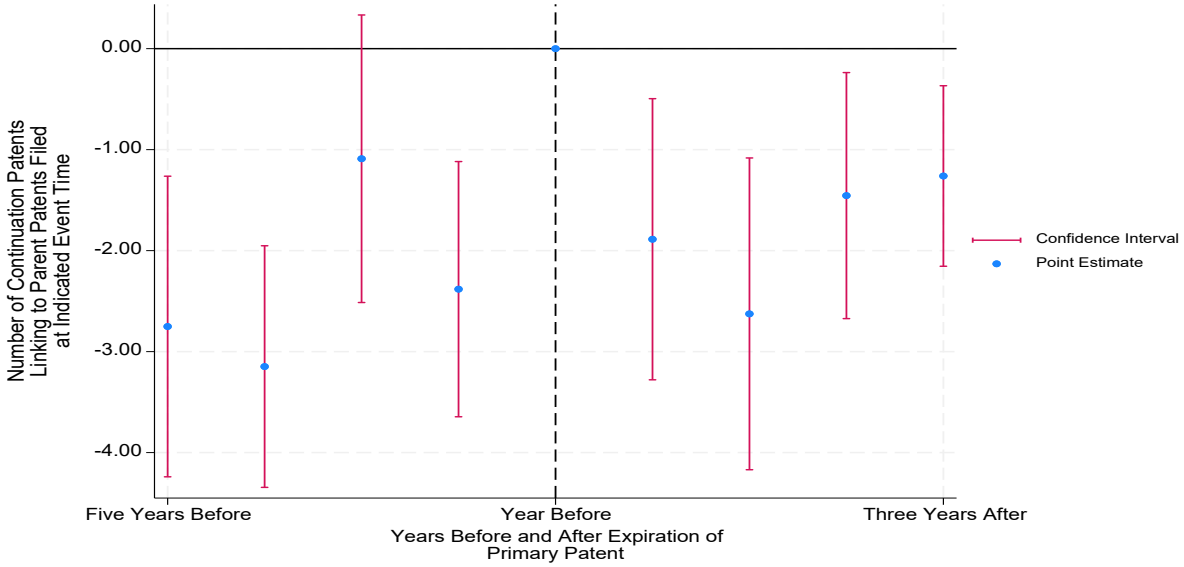



Notes: this analysis replicates that of Figure 5 in the text, but also expanding cohorts to include applications filed until 2021. N = 764 in Panel A and 635 in Panel B.

Continuation Thicketing Analysis

To test the prediction that those non-continuation patents filed immediately before primary patent expiration are more likely to be parents of later filed continuation patents, we estimate a specification similar to that underlying the EPO analysis from Figure 5, but where the dependent variable is now the number of continuation patents later filed whose parent is the focal non-continuation patent filed in the relevant event time. We show results from our most robust approach that includes the control drugs from Figure 4 / Panel B within each layer of the stack. Our coefficients of interest are again the interaction between the treatment-drug indicator and the event-time dummies, which we plot in Figure A17. As demonstrated, we find that among those original non-continuation patents filed in the period of time leading up to the primary patent's expiration, those filed immediately prior to the relevant expiration date are those most likely to be the parent of a subsequent continuation filing.

Figure A17. Number of Continuation Patents Linked to Non-Continuation Parents in Years Leading up to and Following Primary-Patent Expiration, by Timing of Filing of Non-Continuation Parents



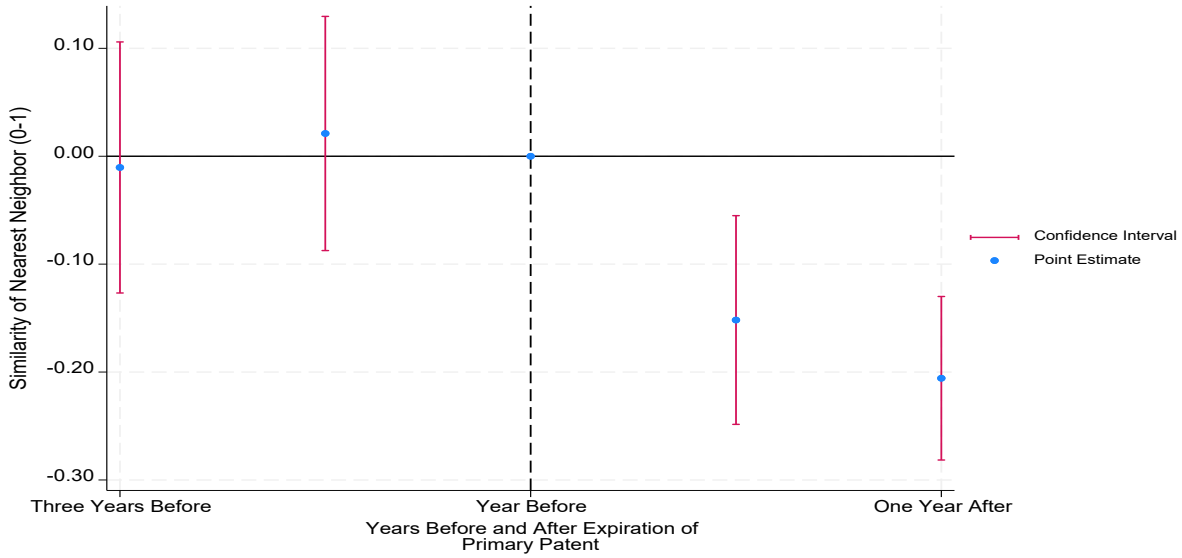

Notes: this analysis estimates a specification analogous to specification (3) where the unit of observation is a given non-continuation patent filed and where the outcome variable is the number of continuation patents that are later filed and whose parent patent in the focal non-continuation patent.

Semantic Similarity Analysis

To complement our analyses in Figure 5 and Figure A17, we consider a related exercise using an alternative innovativeness measure associated with those patents filed in the event window surrounding the primary-patent expiration. For these purposes, we turn to data produced by Whalen et al. (2020), which creates metrics illuminating the textual similarity—based on patent documents—between patent-patent pairs. Similarity scores scale from 0 (least similar) to 1 (most similar). Using their data, we determine how similar the focal biologic patent is to its most textually similar neighbor. We then estimate a version of specificaiton (2) using this similarity score as the dependent variable, where the unit of observation is a given drug-patent pair filed within the event window.

This analysis confronts a similar truncation challenge to that confronted by the EPO analysis insofar as (i) the Whalen data is only based on patents granted until 2019 and (ii) we need to provide time for filed patents to reach the grant stage. Ultimately, these factors leave us unable to considerwith reliability application years past 2017. For this reason, we focus this analysis on a tighter two-year event window around the year prior to primary-patent expiration, focusing on the 2013-2016 event cohorts. We present the result of that analysis in Figure A18.

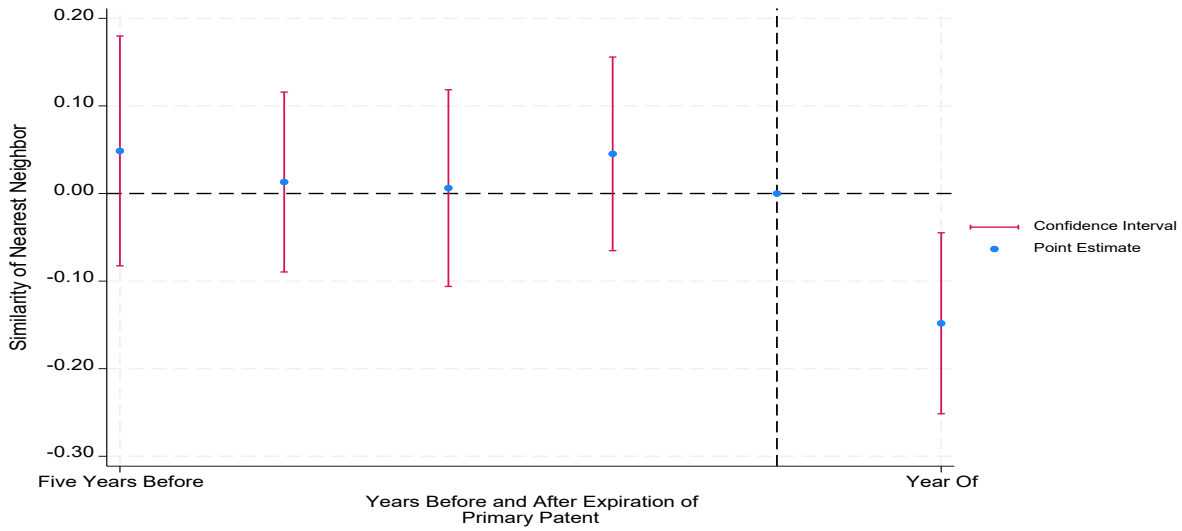
Figure A18. Semantic Similarity Score of Nearest Neighbor, by Years Leading up to and Following Primary-Patent Expiration




Notes: this analysis estimates a specification analogous to specification (3) where the unit of observation is a given drug-patent pair filed at the indicated event time and where the outcome variable is the semantic similarity score of the patent's nearest neighbor, following Whalen et al. (2020).

In Figure A19, we focus specifically on the pre-period and estimate more pre-expiration event years, drawing on the 2015-2017 primary-expiration cohorts (allowing observation of patents filed post-2010 and prior to 2018 to address the stated truncation concerns). We estimate a sharp drop in semantic similarity at the moment of the primary-patent expiration.

Figure A19. Semantic Similarity Score of Nearest Neighbor, by Years Leading up to and Following Primary-Patent Expiration (Focusing on Pre-Period)




Notes: this analysis is analogous to that estimated in Figure A18 though adding more pre-primary-expiration years and focusing on the pre period.

The results from this similarity analysis suggest stability in the similarity scores of patents filed leading up to primary expiration with a sharp drop in similarity at the moment of primary patent expiration, suggesting that patents filed in the pre period are more similar to existing patents. To the extent similarity scores proxy for innovativeness, this analysis is partially consistent with the results from the text. It certainly reinforces a non-innovation gaming story. However, Figure 5 in the text found evidence of both non-innovative gaming and legitimate innovation that is strategically timed with reference to the primary patent expiration. Ultimately, we choose to prioritize the EPO analysis as it provides a more logical innovativeness flag given that the EPO and U.S. Patent Office apply functionally similar patentability criteria that tracks patent novelty and non-obviousness. Textual similarity is likely to be related to this consideration but in less conceptually precise way.

Additional reference:

Whalen, Ryan, Alina Lungeanu, Leslie DeChurch, and Noshir Contractor. 2020. "Patent Similarity Data and Innovation Metrics," Journal of Empirical Legal Studies 17(3): 615-39.

Analysis of Affordable Prescriptions for Patients Act (APPA)

In attempting to place limits on thicketing and evergreening by biologics manufacturers, the APPA divides patents into three categories: (1) patents filed with the U.S. Patent & Trademark Office within four years of the biologic's FDA approval, (2) patents granted after the biologic manufacturer submits its 3A list to the biosimilar applicant (which is a list exchanged by a biologics manufacturer and a biosimilar producer during the "patent dance," a pre-litigation dispute-resolution process), and (3) biologics patents that do not fall into the first two categories. There are effectively no limits on asserting the first type of patent in litigation. The APPA allows up to 10 types of patents in the second category to be litigated and up to 20 types of patents collectively between the second and third categories.

We apply these APPA parameters to our novel biologics patent database to simulate the extent to which the APPA would limit biologics litigation. For these purposes, given that the vast majority of biologics in our database have not engaged in the patent dance (at least yet), we ignore the second category and effectively view the APPA as imposing the following restriction: biologics manufacturers can assert as many patents as they want that were filed within four years of their FDA approval but are limited to only twenty patents past that point. As a preliminary note, the reported simulated effects shed light on the effects of the APPA under an assumption that biologics manufacturers will not alter their patenting practices in response to the APPA. In that light, these results are best seen as a parameterization of the strength (or potential effect) of the law itself rather than its actual effect.

As demonstrated by Table A3, we find that 13.7% of biological drugs have at least one patent that could not be asserted under the APPA, 10.6% of biological drugs have more than 5 patents that could not be asserted under the APPA, 8.3% of biological drugs have more than 10 patents that could not be asserted under the APPA, and 5.5% of biological drugs have more than 20 patents that could not be asserted under the APPA.

Table A3. Percentage of Biologics Implicated by APPA

| | At Least 1 Patent | More Than 5 Patents | More than 10 Patents | More than 20 Patents |
|---|---|---|---|---|
| Percent of Biologics with the Indicated Number of Patents Implicated by the APPA | 13.7% | 10.6% | 8.3% | 5.5% |

Notes: Percentages based on 515 approved therapeutic biologics.

Next, we calculate the percentage of an average biologic patent portfolio that cannot be asserted in patent litigation with the APPA restrictions. We also do the same considering various alternative policy parameters. The first two such alternatives track the current APPA structure by providing no limits on the number of patents that can be asserted if filed within four years of the biologic's approval. However, these alternatives differ from the APPA on the number of patents that can be asserted if filed four years after the biologic's approval. In the first alternative , we limit the manufacturer to 10 patents instead of 20. In the second, we prohibit the assertion of patents filed four years after the biologic's approval altogether. In the third alternative, we restrict assertions to patents filed before the biologic's approval. The results of this new exercise are reported in Table A4.

Table A4. Percentage of Average Drug Portfolio that Cannot Be Asserted in Litigation Under Various Policies

| | APPA: Can assert any patents filed within 4 years of biologic's approval and up to 20 patents thereafter | Alternative 1: Can assert any patent filed within 4 years of biologic's approval and up to 10 patents thereafter | Alternative 2: Can assert any patent filed within 4 years of biologic's approval and no patents thereafter | Alternative 3: Can assert any patent filed before biologic's approval and no patents thereafter |
|---|---|---|---|---|
| % of Average Drug Portfolio that Cannot be Asserted in Litigation | 4.8% | 9.9% | 37.3% | 55.4% |

Notes: Percentages based on 515 approved therapeutic biologics.