Competition and Innovation Revisited: A Project-Level View

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Abstract

We offer a first-ever direct test of the mechanism behind Aghion et al.'s (2005) inverted-U competition-innovation relationship. FDA awards of Breakthrough Therapy Designations (BTDs) on drugs serve as instruments for stochastic shifts in their model between neck-and-neck and unleveled status of that drug's product (therapeutic) market. Rivals' development hazards on their shocked projects – their innovation – increase when the shocked market is ex-ante less competitive, and vice-versa. We highlight several drivers of rival responses underlying the inverted-U, including high exposure to the shocked market, as well as rival usage of other-BTD methods-of-action (technologies).

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The relationship between competition and innovation is of crucial interest to academics, regulators, firms, and consumers. It carries the potential for both company and individual windfalls, it can guide policy, and has broad economic and societal influence. Yet the shape of that relationship remains inconclusive with oft-conflicting empirical results,[1] as well as varying theoretical perspectives.[2] We offer a new test of the workhorse model by Aghion et al. (2005) that delivers the theorized inverted-U relationship between competition and innovation.

Our unique perspectives are two-fold. First we address a key concern with extant tests of the relationship; they are typically conducted at the firm-level. This implicitly ignores heterogeneity in firm product-market exposures, which is an increasing concern (Hoberg and Phillips (2021)). In other words, both competition levels and firm innovation efforts may vary across the product markets they face, potentially masking firm-level estimates of the relationship. We avoid this "aggregation" problem by studying the relationship at the granular project-level.

Second, we side-step challenges to identifying *exogenous* variation in competition that would (nevertheless) be expected to influence firms' innovative activities. Instead, we aim to test the key mechanism driving Aghion et al.'s (2005) main result that innovative activity by firms varies with both the product market's competitiveness and whether that market is "leveled" or "unleveled". Put simply, we identify exogenous shocks to a product market's "level-ness" and test whether competitors in that market vary their innovative responses depending on that market's ex-ante competitiveness.

Specifically, we study shocks to product markets in the drug industry. On July 9, 2012, the Food and Drug Administration (FDA) introduced a new expedited evaluation pathway named the Breakthrough

[1] Hombert and Matray (2018), Hoberg, Li and Phillips (2021) and Autor, Dorn, Hanson, Pisano, Shu (2020) document negative relationships between competition and innovation. Phillips and Zhdanov (2012), and Bloom, Draca and Van Reenen (2016) document positive relationships.

[2] For the negative relationship, see Schumpeter (1943), Salop (1977) Dixit and Stiglitz (1977), Romer (1990), Aghion and Howitt (1992), and Grossman and Helpman (1991). The contrasting view of a positive relationship is presented in Hart (1983) via agency considerations, and by Aghion, Harris, Howitt, Vickers (2001) with step-by-step innovations. Aghion, Bloom, Blundell, Griffith, Howitt (2005) derive an inverted-U relationship.

Therapy Designation (BTD) program. It is designed to facilitate and accelerate the approval of therapies that have demonstrated substantial improvements over available treatments in a given therapeutic area (a.k.a. disease indication).[3,4] This description of BTDs and its recipients fits neatly into the characterization of leaders – who are a step ahead of competitors in the same industry – in the Aghion et al. (2005) model. Empirically, we use BTD events as time-varying cross-sectional shocks to therapeutic areas (i.e. product markets), which plausibly unlevel said markets. We then examine the project-level innovation responses of rivals (who are developing drugs in that same market), and how these responses are moderated by the ex-ante competitiveness of the shocked market.

There are two key advantages to our approach. First, pharmaceutical data are available at the product/project level, with each project targeting a specific product market (therapeutic area). This enables measurement of both competitive environment and innovative activity with the granular detail necessary to avoid aggregation challenges.[5] Second, the BTD events are plausible surprises to the competitors whose innovation responses we seek to explain. Moreover, parallel trends analysis indicates no [anticipatory] acceleration of innovation activity in advance of BTD shocks on average in that therapeutic market. These characteristics of the data help us to draw a link between BTD events and the stochastic variation in market level-ness modeled in Aghion et al. (2005). Combined with our analysis of the mediating effect of market competitiveness on rival innovation response, we offer a unique direct test of the mechanism behind their model, at the project-level.

We begin our presentation of results with a simple event study. BTD firms experience significantly positive abnormal stock returns, and rival firms experience significantly negative ones, around BTD

[3] See Sherman (2013), Hermosilla (2022), and Chandra et al. (2021).
[4] We use the terms disease, indication, and therapeutic area interchangeably to refer to the condition that a drug (project) targets. Our preferred term is therapeutic area since it most closely connotes a product market space.
[5] We illustrate the effect of aggregation across projects within firms on the competition-innovation relationship, in section 4.5, Table 9. It renders the correlation null.

announcement dates.[6] This supports our contention that such events are surprises to treated firms. It also implies a distinct advantage to the BTD-receiving drug and concomitant disadvantage to rival drugs being developed for the same therapeutic market. In the context of the Aghion et al. (2005) model, the industry becomes unleveled, with the BTD-receiving firm considered to now be a step ahead (i.e. a leader) of their non-BTD-receiving rivals (i.e. laggards or followers).

Turning to these now-laggard rivals' responses, we measure their innovation activity by whether they develop their phase-II projects that reside in the BTD-shocked therapeutic area, to reach phase-III. Phase-II development is a significant decision, involving human trials as well as much higher expenditure than phase-I. We specifically compare shocked drug development hazards (from phase-II to phase-III) with unshocked drug development hazards (also from phase-II to phase-III). The hazards of BTD-shocked drugs are significantly lower.

However, the model in Aghion et al. (2005) generates an inverted-U relationship between competition and innovation by discriminating between innovative responses to un-leveling shocks in either less or more competitive markets. When we empirically separate the treatment effect for ex-ante high vs. low competition markets, the hazard-lowering effect is concentrated in ex-ante more competitive therapeutic markets. By contrast, when the BTD-shocked market is ex-ante *less* competitive, BTD-shocked rivals' phase-II to phase-III project continuation hazards are *higher* than those of controls.

These primary results directly support Aghion et al.'s (2005) hypothesized mechanism driving the inverted-U competition-innovation relationship. They posit that when there is not much product market competition, the industry will be quick to leave the unleveled state. The higher continuation hazards of rivals post-shock (i.e. after unleveling), in markets that were ex-ante less competitive, supports this prediction. On the other side of the inverted-U, they argue that "when competition is initially very high there is relatively little incentive for the laggard in an unleveled state to innovate." The lower post-shock

[6] Our event study results only apply among publicly-traded drug companies. Our full sample includes private firms.

continuation hazards of rivals in markets that were ex-ante more competitive, supports this prediction as well. Given our contention that the BTD shock unlevels the industry, and the implied designation of rivals as laggards, we see both effects as predicted.

We further explore the economic incentives driving rival responses to BTD events. On the more competitive markets side of the inverted-U, they reflect variation in rival concern due to the BTD shock of a part of their overall business model (portfolio of drug projects). First we show that more "exposed" rivals – through concentration of their drug project portfolio in the BTD-shocked market – drive the reduced continuation hazard in more competitive markets. They discern significant threat to their business model and adjust resource allocation. Second, the reduced continuation hazard in more competitive markets is stronger when the rival's focal project has a longer development time. Given the expected rapid approval of the BTD-recipient drug, rivals recognize that the BTD drug is likely to dominate the market by the time the rival's own project is potentially approved. This further discourages resource expenditure.

On the lower competition side of the inverted-U, we show one potential mechanism behind acceleration of phase-II shocked projects to phase-III; use of a BTD-approved "technology" (method-of-action). When a shocked rival's drug targets a less competitive market, there is still potential value to catch-up. But the rival's drug will need to show its value (and also get approved by the FDA). Adopting a technology that was used in a previously-BTD-receiving drug (even if that drug belongs to a different company), is a viable strategy.[7] We find that shocked rival projects residing in less competitive markets, but which also adopt a previously-designated-BTD-drug's technology, accelerate post-shock. The rival noted the efficacy of this technology by observing the regulator's positive signal (BTD) and accelerated their own project using the same technology.

We address interpretative concerns with our results in several ways. First we recognize that our

[7] The shocked rival may choose to develop that technology organically, or it may license it. We do not distinguish between the two strategies.

contribution relies on the importance of heterogeneity in innovation across markets within firms. Therefore, we explore potential *reallocation* of firm resources towards innovation in other markets. To clarify the effect of product market competitiveness on rival response to BTD (i.e. unleveling) shocks when firms reallocate resources, we conduct two more explorations. First we study the continuation hazards of shocked rivals' *other* (i.e. unshocked) phase-II projects. When the rival was highly exposed to the shock, they accelerate their unshocked projects only if those projects reside in less competitive markets. Second, we study new drug project initiations (development stage) by these BTD-shocked rivals. The new drug project initiations tend to be in less competitive markets, particularly when the BTD-shocked drug's market was highly competitive. Overall, reallocation of resources by shocked rivals is consistent with the predictions in Aghion et al. (2005).

Another interpretive concern is whether BTD shocks should *always* be viewed as unleveling a market. If a therapeutic market has multiple drugs in it, and some are FDA-approved for sale while others are still in trials, such a market may reasonably be considered unleveled. Then the effect of the BTD shock is less clear. If the BTD is received by a drug project that is owned by a firm that also has an FDA-approved drug for sale in that same market, the [further] unleveling interpretation is likely still valid. By contrast, if the BTD is received on a drug project owned by a firm with no FDA-approved drugs for sale in that market, then it is possible that therapeutic market *levels* (instead of unleveling). To set aside this latter possibility, we re-run our primary test for two sub-samples where the therapeutic market is likely ex-ante leveled. These include markets where all firms operating in it have an approved-for-sale drug in that market, and the opposite (i.e. none have an approved-for-sale drug in that market). Our primary result is robust. We also support another implication of Aghion et al. (2005) with our sub-sampling of such ex-ante level markets; the vast majority of them are ex-ante less competitive.

A third interpretation concern stems from recent work by Hermosilla (2022). He concludes that the BTD program encourages drug companies to "chase" the designation with newly introduced projects.

If the project fails to obtain a BTD then it is abandoned quickly. If our results are due to these phase-II projects that were introduced after the first BTD in a therapeutic area, then they could be due to inferior project quality instead of due to competitive effects. We address this alternative interpretation by re-estimating the primary relationship on an alternative sample; rivals' shocked phase-II projects that were in place *before* the first BTD arrived in that market. Again our inferences persist.[8]

Finally, we offer a litany of robustness checks in our internet appendix. These include alternative proxies for therapeutic area ex-ante competitiveness, as well as more restrictive matching of shocked drug projects with controls. Our conclusions persist.

We make substantive contributions to several literatures. Primarily, we are (to the best of our knowledge) the first paper to directly test the mechanism underlying Aghion et al.'s (2005) inverted-U workhorse model. Second, we run these tests at the corporate project level. Combined, we offer primary empirical support for the inverted-U relationship between competition and innovation, uncontaminated by two typical complications. Other empirical work (see footnote 1) potentially suffers from either or both.[9]

We also contribute to a recent spate of papers using pharma data to study corporate behavior at the project-level. Krieger (2021), as well as Krieger, Li and Thakor (2022) examine the impact of negative competitor outcomes – public health advisories (PHAs) and product failures respectively – on rival project development. Cunningham, Ederer and Ma (2021) find that firms thwart future competition by acquiring competitors and discontinuing their similar drug projects that were under development. Lo and Thakor (2022), as well as Li, Lo and Thakor (2021), study changes in law that affect competition and their influence on innovation spending and financing. Kao (2022) studies disclosure decisions on clinical trials outcomes

[8] Hermsoilla (2022) studies a mechanism behind firms "chasing" a BTD, which he labels policy exposure. In our robustness checks we conduct double-sorts including policy exposure to further allay concerns that our results are due to this alternative incentive. Our inferences persist.

[9] Note in particular our later evidence that firm-level aggregation can mask relationships.

as a function of competition. Chandra, Kao, Miller, and Stern (2022) study BTDs, but only the effects on BTD-recipient drug outcomes (time-to-market and safety). None of these papers offer direct tests of the mechanism underlying Aghion et al. (2005), nor do they (all but one) utilize the setting of BTDs.[10]

Finally, we speak to the literature on rival responses to entry threats.[11] Extant work finds mixed evidence on whether incumbents are more likely to deter or accommodate entry. However, none of the listed papers consider within-firm cross-sectional variation in product market competitiveness, exposure to shocks, and responses. We show that these considerations matter.

1. Drug Industry Data and Markets

We require information on company innovation investments by product market, as well as the competitiveness of each market the company operates in. Pharma data offers insights along both dimensions. As Krieger (2021) explains, drugs require testing through multiple stages, eventually climbing through human-clinical trials before FDA approval for widespread use. Each stage of progression is considered a milestone (e.g., moving from phase-I to phase-II of clinical trials) and project milestones data are available through various sources.[12] Each drug *project* also targets one disease indication. We use this information to assign drug projects to product markets. We then determine each market's competitiveness based on the totality of projects targeting that disease.

1.1. Base Drug Development and Manufacturer Data

Our drug development data comes from Clarivate Analytics' Cortellis Competitive Intelligence™.

[10] Also, Guedj and Scharfstein (2004) find that smaller biotech firms are more likely to advance lower quality phase-II clinical trials, relative to large pharmaceutical companies. And Aboulnasr et al. (2008) study firm-level responses to competitor receipt of priority review designation. Neither test Aghion et al. (2005) and they both aggregate to the firm-level.

[11] See Walmart entry (Khanna and Tice 2000, 2001), airline entry (Goolsbee and Syverson 2008, Parise 2018, Kwoka and Batkeyev 2019, Ethiraj and Zhou 2019), foreign products entry (Frésard and Valta 2015) generic drug entry (Tenn and Wendling 2014), bank entry (Tomy 2019), and Google's entry into the app market (Wen and Zhu 2019).

[12] Particularly for phases-II and higher in human clinical trials, since FDAAA in 2007. See Aghamolla and Thakor (2021) as well as Kao (2022).

Cortellis is an industry competitive repository of pharmaceutical innovation and has been used in recent papers (e.g., Krieger (2021), and Hermosilla (2021)). The full dataset of drugs developed for US markets includes detailed development milestone and ownership information on over 14,000 drugs and 30,000 drug projects developed by over 5,000 firms.[13]

Our sample analysis period is 2010q1 – 2020q1. The beginning date allows for about three years of data before the first approved BTD, which occurred in late 2012. We retain only drug projects developed for U.S. markets and we drop those with missing key development dates. We also drop "zombie" projects as defined by Krieger (2021). Finally, we drop all drug projects originated by educational or not-for-profit research institutions.[14] As section 3 describes, our primary analysis focuses on phase-II drug projects and their continuation to phase-III. Here we present the broad sample construction.

Cortellis lists all current and past owners of a drug. It further indicates whether a change in ownership has occurred (drug owner acquired, spun off, divested, restructured, or had operated as a subsidiary under another firm). However, Cortellis does not always identify the dates on which ownership has changed. To establish drug project ownership dates across all firms involved in developing a drug project, we match the Cortellis data to SDC Platinum's M&A data.[15]

We combine drug and firm data to create a panel with observational level of drug-project-quarter. We allow a drug project's characteristics (e.g., patent coverage status, stage of development, etc.) and ownership to change over time. The panel includes 29,043 drug projects developed by 4,337 firms from 2010q1 through 2020q1, or 498,183 drug-project-quarter observations.

1.2. ICD-10 Therapeutic Areas

A drug indication is the medical condition that a drug is meant to treat. Cortellis reports drug

[13] Recall that a single drug may be used in multiple projects, with each project targeting a different medical condition (i.e., indication). We therefore define a drug project as a drug-indication combination.
[14] These institutions have different sources of funding (e.g., NIH), and therefore, different incentives to innovate. Drug projects originated by these institutions are only included once they are licensed to a corporation.
[15] Our specific ownership assignment procedure is described in Online Appendix I.B.

projects by indication. However, these indications are descriptions that can come from multiple data-sources driving Cortellis' data collection process.[16] These descriptions of the same medical condition are not always consistent across such sources.[17]

To identify potentially competing drug projects, we perform a grouping analysis. We map Cortellis indications to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems classifications (herein ICD-10 codes) at the second subchapter level.[18] These codes define a therapeutic market. Then we identify all drug projects targeting indications inside the same ICD-10 market, as competing ones. Our final count of unique ICD-10 therapeutic markets is 1,295.

1.3. Therapeutic Market Competitiveness

We define our competition measure as the number of drug projects (in any stage of development) in an ICD-10 market, in each quarter.[19] We choose this project-count-based competition measure over other sales-based competition measures for several reasons. First, it allows us to examine the overall level of development activity within a therapeutic market. Since drug projects often span several years before regulatory approval, *sales-based* competition measures do not incorporate information on a significant portion of the development activity. This is particularly relevant for firms developing not-yet-approved projects but that are expected to compete for pharmaceutical sales upon approval.[20] Second, sales-based competition measures are subject to measurement error since sales are reported at the aggregated drug level, and most approved-for-sale drugs target several markets. This complicates the calculation of the overall contribution of each market to the drug's total sales. Finally, drug prices are normally reported on

[16] Cortellis collects drug development information from conferences, firm financial statements, and public resources (e.g. ClinicalTrials.gov).
[17] For example, the two Cortellis indications "hsv infection" and "herpes simplex virus infection" refer to the same medical condition.
[18] We consult a clinical pharmacist to find concordance between Cortellis indication names and the ICD-10 diagnostic codes at the second subchapter level. Online Appendix I.A provides details, and also reports on robustness of results to other established therapeutic market classification systems. Our inferences persist.
[19] See too Krieger (2021), and Cunningham et al (2021).
[20] Several papers show that firms pay particular attention to competitors' projects under development (e.g., Kao (2022) and Cunningham et al (2021)).

a list price basis and do not adjust for rebates, further complicating measurement of drug revenues within a therapeutic market.[21]

2. Breakthrough Therapy Designations as the "Unleveling" Mechanism in Aghion et al. (2005)

2.1. Model Implications

Aghion et al. (2005) develop the inverted-U relationship between competition and innovation in several steps. They begin by specifying two types of sectors in an economy: leveled (neck-and-neck) sectors where two competitors are at technological par with each other; and unleveled sectors with a leader that is technologically one step ahead of a laggard (follower). The incentives to expend resources on R&D - to innovate - vary with the type of sector. When the sector is neck-and-neck, R&D expenditures towards innovating may enable a competitor to escape competition; while in unleveled sectors, laggard R&D-to-innovate may allow them to catch up. In both cases there is uncertainty, with firms moving forward one technological step, with Poisson hazard rate positively related to expenditure.

There are two key links between competition and innovation. Within a sector, the model's Proposition 1 governs the relationship. Firms in a neck-and-neck sector see a positive equilibrium relationship between competition and innovation. Intuitively, a firm sees larger gains post-innovation relative to pre-innovation (i.e. after "escaping neck-and-neckness"), when competition is higher. By contrast, in unleveled sectors more competition discourages R&D expenditures towards innovation. This "Schumpeterian" effect is due to greater competition reducing rents, and thereby the payoff to laggard catch-up. The gap between post-innovation and pre-innovation rents decreases with competition.[22]

[21] Nevertheless, our main result is robust to using an alternative – much noisier – sales-based HHI concentration measure calculated from Medicaid sales data. These results are reported in Table B2 of the appendix. Furthermore, Online Appendix Section I.E.2 provides details on the construction of this sales-based concentration measure and shows that HHI (from noisy data) is significantly negatively correlated with our main competition measure. This lends further credence to our use of the *more precise* project-count measure of competition.

[22] This latter result is due to the model's assumption that leaders cannot move more than one step ahead. So innovation is done by the laggard and can only result in catch-up.

The second link is cross-sectional and is presented in Proposition 2. Aghion et al. (2005) label it the composition effect. Less competitive sectors will most often stay leveled while more competitive sectors tend to remain unleveled.

The inverted-U in their model is the aggregate economy-wide cross-sectional outcome from Proposition 2, but the incentives described in Proposition 1 can be considered drivers. As Aghion et al. (2005) describe it, when competition is low there is little incentive for neck-and-neck firms to innovate (which is why those sectors tend to remain leveled). But this further implies that if a sector unlevels through a shock, it will see accelerated innovation to return to a leveled state. By contrast, ex-ante more competitive sectors tend to remain unleveled because laggards see little incentive to expend resources to innovate (catch-up) when post-innovation rents are meagre in such sectors. In summary, sectors respond differently to shocks that unlevel them, depending on their ex-ante competitiveness.

2.1.1. Logic of the Test

Our tests are built on this logic. We require a shock that suddenly unlevels a sector and then we explain the sector's innovation response as a function of ex-ante competitiveness. We rely on BTDs to instrument such shocks. Since the stochastic variation in the model comes from the relationship between research intensity and technology gap, it's important that BTDs – which create the gap – be quasi-random with respect to ex-ante innovation. We submit that they are. As we discuss below (in 2.2), the breakthrough designation is based on FDA decision about the improved treatment effects. It is not necessarily driven by ex-ante R&D in the sector.[23] Also, we show in section 2.4 that BTDs are surprises. Finally, in section 3.3, parallel trends indicate no anticipatory increase in innovation within the therapeutic area, pre-BTD.

[23] Put differently, sometimes much research is done and nothing comes of it while other times one stumbles across a magnificent discovery.

2.2. BTD Program Salient Institutional Characteristics

The BTD program specifies two criteria for award: the recipient drug must target serious or life-threatening conditions; and it must demonstrate substantially better treatment effects than existing therapies. The latter is stringent. Submitted results from phase-I or phase-II clinical trials are carefully assessed by FDA staff. Preliminary clinical evidence should show a clear advantage over available therapy. The closest other FDA program for expediting drug projects – the Fast Track program – requires only mechanistic rationales instead of clinical results to support claimed supremacy[24] (see Hermosilla, 2022).

Another key element of the BTD program is its early-decision setting. Figure 1 illustrates this in the context of the drug development process. BTDs may be requested as early as concurrent with an Investigational New Drug (IND) application, and typically before the end of phase-II. The timing is important because it allows for meaningful impact of BTDs on approval speed – one of the goals of the program. This further implies that widespread knowledge of clinical trial outcomes (before the BTD announcement) is unlikely, supporting the surprising nature of the announcement. Finally, while the BTD program is the fourth addition to the FDA's expedited approval pathway programs, it tops the ranking in terms of where FDA resources are prioritized (Senior (2013)). Taken together, these characteristics align with Aghion et al.'s (2005) characterization of stochastic unleveling in a product market and the BTD recipient being a leader (with rivals as laggards).[25]

2.3. BTD Event Data, Recipients, and Rivals

We obtain BTD drugs and grant dates from the Friends of Cancer Research (FOCR) website.[26] The

[24] Further evidence of BTD exclusivity is seen in the lower success rate on applications. While about 65% of FTD applications are approved, only 35% of BTD applications win designation.

[25] So too is the evidence we present in Online Appendix I.C.3 detailing the views of patients, doctors and the industry, of BTD-awarded drugs. In summary, physicians are more likely to prescribe approved BTDs relative to alternative therapies, and patients are more likely to request them. Since demand for pharmaceutical products is mostly driven by physician office visits, BTD drugs often dominate the therapeutic market they target. For example, Merck's Keytruda claimed over 80% of sales in the non-small cell lung cancer market one year after its approval.

[26] https://www.focr.org/breakthrough-therapies

site identifies each BTD drug's name, the announcement date, the sponsoring firm and the indications for which the BTD was granted. We manually match each BTD award to its corresponding drug project in the Cortellis data.[27] If a BTD is granted to more than one drug or more than one firm, we treat each as a separate BTD. Finally, we drop (5) BTDs that were rescinded, from our sample.

Table 1 provides summary statistics for the BTDs in our sample. We identify 253 unique BTD designations, awarded to 272 drug projects in 145 ICD-10 markets.[28] There are 113 BTD-receiving firms in our sample; 83 public and 30 private. Most BTDs are awarded to larger publicly traded firms and to firms with already-FDA-approved drugs on sale in at least one market.[29]

We define a rival as any firm that is actively developing at least one drug project in the BTD-shocked ICD-10 market, but who does not have a BTD-awarded drug in that market.[30] We focus the bulk of our analysis on rivals' drug projects and their development.

2.4 Stock Price Reactions to BTD Events

To establish that BTD grants are a surprise – positive for BTD firms and negative for rival firms, we conduct event studies around BTD announcements. The sample includes BTD-recipients, rivals and controls.[31] Control firms do not have any drug projects residing in the BTD drug's ICD-10 market.

We calculate abnormal returns using a market model with parameters estimated over [−271, −21], relative to the BTD grant announcement date. The abnormal event return (CAR) is calculated over the

[27] Online Appendix I.C.1 provides details on this matching process and the cross-validation with other data sources.
[28] Note that the same BTD can be awarded to several drug projects or to several firms. This is why some subsamples add up to more than 253. Furthermore, some precommercial firms became commercial at a later date once they received FDA approval for one of their products. Such an occurrence results in counting the same firm as both commercial and precommercial, if it receives a BTD in both periods. See for example Clovis Oncology.
[29] Online Appendix I.C.2 provides both time-series and cross-sectional visualizations on BTD awards. Figure I.C.2.A displays the distribution of awards by year. Figure I.C.2.B presents the distribution of awards by therapeutic market. The latter shows that most designations were granted in the cancers and neoplasms markets (about 47% of all awards). This is not surprising given that the program requires designated drugs to target serious or life-threatening conditions. Furthermore, most drugs under development target some type of cancer (e.g., 33% of our sample drugs).
[30] It is feasible that a rival in one market may possess a BTD drug in a different market (where we would not include them in the set of rivals).
[31] All firms in this analysis must be publicly traded, somewhat reducing our sample size in this section.

three-trading day window [-1, +1] relative to the same date. We drop observations where the firm had other important corporate events around the BTD announcement.[32] Finally, we winsorize CARs at the 1% and 99% levels for analysis and reporting. The final sample includes 189 BTD firm-dates, 3,591 rival firm-dates, and 89,014 control firm-dates.

Table 2 presents OLS regression results of the 3-day abnormal event-returns (CARs) on variables that capture a firm's status in the shocked therapeutic market. Column 1 confirms that BTD announcements are good news for recipient firms (1.6%) and bad news for rival firms (-0.2%), both statistically significant relative to control firms.[33] Column 2 illustrates that these average effects are concentrated in the sub-samples of precommercial firms, with significant coefficients on the interactives of the *Precommercial* dummy with the *BTD Firm* and *Rival Firm* indicators. Columns 3 and 4 present regression results on separate subsamples of BTD firms and rival firms, respectively. The results in the last two columns confirm the finding in Column 2 that the average effect is primarily driven by precommercial firms.[34] Overall, we conclude that BTD events are surprises.

3. Empirical Design, Development Hazards, and Parallel Trends

This section lays out our main testing approach. Section 3.1 explains the focus on phase-II projects and their graduation to phase-III to proxy innovation, and describes the analysis sample. Section 3.2 presents the hazard model. Section 3.3 presents time trends in the development rates of BTD-shocked

[32] The large sample (92,000 firm-dates) makes manual search for confounding press releases difficult. Therefore, we restrict our search to observations with CARs in the top and bottom 5% of the distribution (roughly, CARs greater than 15% or less than -15%). We search business press releases for these firms around the BTD announcement date. We drop firm-date observations where an impactful corporate event had concurrently occurred with the BTD announcement, e.g., merger, CEO death, CEO indictment…etc.

[33] Univariate tests of BTD announcement returns without relative comparison to controls are displayed in Table I.D.1 of Online Appendix I.D, and are consistent.

[34] Noteworthy is the choice of fixed effects (FE) across columns. In the first two columns, we include both firm and event FEs. We do not include firm FEs in columns 3 and 4 due to the high number of singletons in these smaller subsamples. Furthermore in column 3, we do not include event FEs for the same reason. We also control for any correlation in the error terms across firms or time by double clustering standard errors by firm and event.

phase-II projects, relative to control (i.e., non-shocked) projects, around BTD events.

3.1. Phase-II to Phase-III Development Continuation – Data and Motivation

Our main analysis relies on the development of drug projects from phase-II to phase-III to proxy innovation. Our reasons mirror Krieger's (2021). First, phase-II is the initial test of a drug's efficacy in humans, requiring significant capital investment.[35] The magnitude of resource dedication aligns with Aghion et al.'s hazard rate of innovation rising in investment amount. Second, phase-II projects have much higher levels of uncertainty relative to phase-III projects.[36] Given such high uncertainty, the information content of a BTD event at this development stage is large. Third, firms are legally required to report their phase-II trial results in a timely fashion, providing a more complete characterization of competing projects and innovation outcomes within a therapeutic market.[37]

Our data panel formation begins with all projects that report phase-II trials at any point in time between 2010q1 and 2020q1 (inclusive). We then identify the subset of projects that reside in the same ICD-10 market that experiences BTD entry *at some point* in our sample period. Broadly speaking, these are the potential rival projects.[38] Rival projects are then selected in two distinct ways reflecting time-series criteria. In the broadest selection, all potential rival projects owned by firms that did not have a BTD of their own in that market, are designated as rival projects starting on the BTD event quarter and until the end of the sample. The corollary sub-sample of "never shocked" firms is our control set. Our main tests are based on this broad selection. Our stricter sampling (used in robustness checks) is of these rival projects for up to 8 or 12 quarters after the BTD event quarter. In both cases, non-rival projects (never-

[35] On average, phase-II projects cost between $13 million and $80 million, whereas phase 1 projects cost between $4 million and $8 million (Krieger 2021).

[36] Hay et al. (2014) report that only 16% of phase-II projects are eventually approved vs. a 50% approval rate of phase-III.

[37] The 2007 FDAA act required firms to report the findings from phase-II and phase-III (but not phase-I) trials no later than a year after their completion. Firms that delay the reporting beyond this window are subject to civil monetary penalties of about $10,000 per day.

[38] We drop any phase-II projects of BTD-recipient firms that reside in that BTD-receipt-market. We do so to mitigate the confounding effects of BTD awards on the recipient firm's innovative activities.

shocked, pre-shock, or after the post-shock multi-quarter window closes) serve as controls.

Table 3 presents summary statistics for the full sample of phase-II drug projects. There are 5,194 projects developed by 1,263 firms in 752 ICD-10 markets from 2010q1 to 2020q1. The observation level in the sample is project-quarter and the final panel consists of 62,033 observations. We then divide the sample into two groups; rival projects that eventually experience BTD shocks, and control projects that are never shocked. Panels B and C further partition the sample by low and high levels (above and below the median) of market competition, respectively.

Three key observations emerge from Table 3. BTD-shocked projects are generally less likely to continue phase-II development relative to control projects. This is especially the case in high competition markets. Third, about 80% of BTD shocked projects fall in high competition markets, whereas only about one third of control projects target these markets. This last finding is expected since BTD designations are mostly awarded to the more competitive indications that are serious or life-threatening.[39]

3.2. Hazard Methodology

We label our key independent variable "BTD Shock", which serves as our proxy for a therapeutic market's unleveling. It is an indicator variable set equal to one for rival projects starting on the BTD grant quarter and continuing until the end of the sample; zero otherwise.[40] Our main dependent variable "Development Dummy" is also an indicator, set equal to one in the quarter that a drug project graduates to phase-III, and zero as long as it remains in phase-II.

We follow Krieger (2021) in using a hazard model to estimate the effect of shock events on phase-

[39] Nevertheless, in robustness tests, we confirm that our results are not driven by systematic differences between BTD-shocked - and control - markets. First, we stratify baseline hazards by market in our main tests (more details in section 3.2). This allows the treatment effects to be computed relative to counterfactuals with highly similar market characteristics. Second, we run our tests using subsamples partitioned on high and low competition levels, where differences in competition levels are much less pronounced. Third, Table B1 of the main appendix reports results from a replication of our main tests using two alternative samples that do not exhibit statistically significant differences in competition levels; (see section 5.2 for discussion of these results). Our inferences persist.

[40] Robustness tests where we shut off the Market Shock indicator either 8 or 12 quarters after the BTD event yield similar results and the same inferences.

II project development decisions. A hazard model accounts for binary outcome variables (reaching phase-III or not), variable response times (to reach phase-III), and right censoring (drug development typically lasts several years, implying firms may continue development after the end of our sample period). We use the Cox proportional-hazards model with the *Development Dummy* as our success event. The analysis time is the number of quarters since the start of phase-II for that drug project. Our base specification is:

$$h_{ij}(t) = h_{0j} \cdot exp[\beta_1 * BTD\ Shock_{jt} + X_{ijt}'\boldsymbol{\beta} + \delta_t] \quad (1)$$

where *i* indexes drug project, *j* indexes therapeutic market, *t* indexes the number of quarters since the beginning of phase II, X_{ijt} are time-varying covariates, and h_{0j} is the baseline hazard rate of Phase-II development. We stratify the baseline hazard by therapeutic market using the more general 1st subchapter ICD-10 definition. Since we define BTD shocks (and therefore rival projects) and therapeutic markets (and therefore competition) using the narrower 2nd subchapter ICD-10 codes, stratifying the baseline hazards by the 1st subchapter allows the treatment effect to be estimated relative to three potential counterfactual groups of projects: never-shocked projects in the same 2nd subchapter market that exit before the first BTD shock; projects in the same 1st subchapter market that is never-shocked; and not-yet-shocked projects in the same 1st or 2nd subchapter market before the first BTD shock enters.[41] To summarize, stratifying our baseline hazards allows us to examine the phase-II development rates of recently shocked projects relative to relevant counterfactual rates of non-shocked projects of the same age, clinical stage and (general) market.[42]

Our main focus is on the *BTD Shock* indicator, which captures the effect of BTD entry on a rival

[41] For example, lymphoma (with a 2nd subchapter ICD-10 code of "C85-0") has 3 other related indications: high grade b-cell lymphoma (ICD-10 code of "C85-10"); primary mediastinal large b-cell lymphoma (ICD-10 code of "C85-20"); and non-hodgkins lymphoma (ICD-10 code of "C85-9"). Only the last two indications experienced a BTD shock. This implies that the average BTD treatment effect on the development rates of shocked projects in the "C85-20" and "C85-9" markets is estimated relative to non-shocked projects with the same stage and age, and that reside in the similar 1st subchapter ICD-10 "C85" market (and therefore share many characteristics such as the targeted organ, risk factors, symptoms…etc.).

[42] We find qualitatively similar results if we stratify our baseline hazards by 2nd subchapter ICD-10 codes, or if we do not stratify the baseline hazards at all.

project's hazard of advancing to phase III. We are particularly interested in how this effect is moderated by the level of ex-ante market competitiveness. We include time (year) fixed effects (the δ_t) and we cluster standard errors by drug project.

3.3. Time Trends in Phase-II Graduation Rates Around BTD Events

Our main tests are effectively difference-in-differences estimations, where the first difference is between shocked and control projects, and the second difference is before and after the shock.[43] Our identification assumption is that the BTD event is exogenous with respect to innovation. To provide validation, we construct a test of parallel trends in the response variable – graduation from phase-II to phase-III, between treated and control phase-II projects, prior to treatment. Put differently, phase-II projects in ICD-10 markets that eventually experience BTD entry should have graduation rates *prior to the shock* that are not significantly different from those of control projects; they should only diverge afterwards. Even when competitors are aware of the development of a competing drug, they shouldn't be able to predict whether it will receive the designation. However, If BTDs were predictable, rivals would endogenously adjust innovation-oriented spending before the event.

To execute this test across the full sample of phase-II projects, we create an indicator, *everBTDshocked*, equal to one if a project resides in an ICD-10 market that experiences BTD entry at some point, and equal to zero for control projects. We then run a hazard model (of similar specification to equation 1), on the graduation rates of phase-II projects, using the interaction of *everBTDshocked* with indicator variables for each of the three years before and after BTD entry.[44] We retain the BTD entry year

[43] The variable, *BTD Shock*, is effectively the interactive *Treatment*Post*. In all tests, we include an indicator for markets that are eventually shocked (which would be the *Treatment* variable). *Post*, however, is subsumed by *BTD Shock* since only treated projects have a post shock period (i.e., *Post* is perfectly collinear with *BTD Shock*).

[44] We use year indicators in the interactive, instead of quarter indicators, because phase-II graduation events are exceedingly rare (only 1% of the sample's observations). As a result, some of the quarter-based interactives become noisy, especially in quarters with abnormally higher (or lower) graduation occurrences within groups of shocked and control projects. On the other hand, graduation events are more evenly distributed across years within these two groups of projects, allowing for more informative estimates with comparable levels of variance in each interaction coefficient. Nevertheless, parallel trends with quarter-based interactives display qualitatively similar results in that

(i.e., year t) as our baseline time threshold. However, results are similar if we instead retain the second or third year before BTD entry. To satisfy the parallel trends condition, the coefficients on interactives representing the three years preceding the BTD, should not differ significantly from zero.

Figure 2 displays coefficients plotted from this analysis. The caps on each coefficient cover 95% confidence intervals. All graphs of Figure 2 lend support to our identification assumption; graduation rates of projects that are eventually shocked are not statistically different from those of controls pre-BTD, and they only begin to differ significantly afterwards. Figure 2A plots the interactive coefficients using the full sample. In the first, second and third year after BTD entry, shocked projects are 63%, 62% and 30% as likely to graduate as control projects, respectively. Figure 2B (2C) plots coefficients estimated using the sample of projects in ex-ante low (high) competition markets – i.e. below (above) that of the sample median. The declining hazards appear to be driven by projects in more competitive markets. By contrast, projects in less competitive markets are 60% *more* likely to graduate relative to control projects.

4. Results

This section presents a broad set of results on the effects of BTD shocks on the drug development activities of rivals. The BTD event is treated as an unleveling shock to the therapeutic market that the drug project is targeting. We first examine the effect of these BTD events on phase-II graduation rates of rivals' projects, and how ex-ante therapeutic market competitiveness moderates it. We then explore potential economic drivers of the rivals' responses. The remainder of the section handles interpretive concerns. We describe rival phase-II project responses in *unshocked* markets. We double-check our main results for the sub-sample of ex-ante level markets. We illustrate the aggregation problem in firm-wide estimations. Finally, we examine drug project initiations of BTD-shocked rivals.

the coefficients of the interactive in the quarters before the BTD event are not significantly different from zero, and the differences only begin appearing after the BTD event.

4.1. Phase-II Graduation Rates and BTD Shock Events

Panel A of Table 4 presents results from our hazard specification in equation 1. The results are broadly consistent with the mechanism driving the inverted-U relationship between competition and innovation in Aghion et al. (2005). In column 1 of panel A, the coefficient on *BTD Shock* is -0.318. On average, a BTD shock within a therapeutic market decreases the likelihood that a phase-II project graduates by (1-exp(-0.318)) 27%. Column 2 of panel A suggests that this decrease in likelihood is driven by therapeutic areas with ex-ante higher levels of competition. The coefficient on *BTD Shock* interacted with *Competition* is -0.499 and significant. Among shocked projects, a one standard deviation increase in the therapeutic market's ex-ante level of competition (which equals 1.45), decreases the likelihood of reaching phase-III by [1-exp(1.45*-0.499)], about 50%.

Columns 3 and 4 of Panel A separately explore the "two sides" of the inverted-U hypothesized relationship.[45] When competition is ex-ante low (Column 3), the coefficient on *BTD Shock* implies that rival projects in suddenly unleveled markets are almost twice as likely to graduate (to phase-III) relative to control projects. This result is consistent with the low competition implication in Aghion et al. (2005). When the unleveling (BTD) shock arrives, laggards (rivals) have an incentive to catch up in less competitive markets; they therefore accelerate their existing phase-II projects (in that market).

By contrast, in ex-ante more competitive markets (Column 4), the BTD shock discourages innovation. The relevant coefficient (-0.544) indicates unleveling leads to 40% lower likelihood that rival (phase-II) projects continue development (to phase-III), relative to control projects in markets with similar levels of competition. This too aligns with Aghion et al.'s (2005) model. In high competition markets, unleveling discourages rival innovation since post-innovation rents (the returns to catch-up) are decreasing in product market competition. In other words, the "Schumpeterian effect dominates.

[45] A key benefit to sub-sample analysis is the removal of interactive variables from a non-linear model. See Ai and Norton (2003) for a description of the challenges.

In panels B and C, we run the same tests using an OLS and a logit model, respectively.[46] The results in both panels indicate concordance with the above. However, while the difference in the magnitudes between coefficients in the hazard model and those in the logistic model are small, the differences between the OLS and hazard models are large. This could be due to several reasons. First, the market-stratified sample of the hazard sample estimates the treatment effect relative to those of the most relevant counterfactuals. By contrast, the OLS model estimates the treatment effect for shocked projects relative to *all* control projects (using the portion of variation within the two groups that was not explained by the fixed effects and control variables). Second, coefficient magnitudes can be influenced by the estimation method (non-linear estimation in the hazard and logistic models, and linear in the OLS model). Third, the samples used in Panels B and C are smaller than in Panel A, due to additional sample restrictions needed to control for right censoring. Finally, estimates from linear models are less reliable when the outcome variable has an extreme distribution. Since the outcome variable in Table 4, Development Dummy, is equal to one in only 1% of observations, the coefficient magnitudes of the OLS model must be taken with a grain of salt. Whereas logistic and hazard models do not have the same concern with such outcome variables, which could explain why their magnitudes are comparable.

Overall, this section provides direct causal support for Aghion et al. (2005). BTD events un-level the therapeutic market. Rivals respond differentially to the shock, depending on whether the market is ex-ante more or less competitive. In low competition markets the unleveling (BTD) shock encourages innovation, consistent with the left side of the inverted-U. In more competitive markets the shock discourages rival innovation, in line with the right side of the inverted-U. Our results are consistent across three different estimation approaches as well (hazard, OLS, and logistic regressions).

[46] Unlike the hazard model which controls for right censoring, OLS and logit models do not. We control for the right censoring nature of our data by dropping all phase-II projects that started development after 2018q1 (since phase-II development takes an average of two years, and our sample ends in 2020q1).

4.1.1. Further Tests of Aghion et al. (2005): Event Returns Segmented by Market Competitiveness

Table I.D.2 in Online Appendix I.D presents results from an alternative test of Aghion et al.'s (2005) implications, using firm announcement returns around BTD events *conditional on* the ex-ante level of competition within the BTD-shocked market.[47] Under the model, un-leveling events (BTDs) in ex-ante low competition markets constitute bad news for the disadvantaged rivals and their shareholders; the leader (BTD-recipient) escaped competition and is expected to garner all rents. This is why the rivals in such markets accelerate innovation to attempt catch-up. But the *event return* implication among these rivals is significantly negative.[48] We find so, with these suddenly laggard rivals in ex-ante less competitive markets experiencing -2.4% event returns.

4.2. Economic Drivers of Rival Reactions to BTD (unleveling) Shocks

We next explore firm (likely) motivations to respond to unleveling (BTD) shocks. We begin with recognition that BTDs place rival firms at a competitive disadvantage. In Panel A of Table 5, we examine how their response varies with the extent of exposure to the shocked market. We define a new variable *Shock Exposure*, calculated as the percentage of a firm's total projects that reside in the BTD-shocked market. This firm-quarter level variable (since exposure can vary by quarter) can proxy for a firm's level of concern about their (new) competitive disadvantage.[49] We include this variable as a moderator of the "treatment" effect. The results in Panel A of Table 5 indicate that firms which are more highly exposed to the shock are significantly less likely to develop their phase-II projects in that shocked market. Furthermore, this result is pronounced in shocked markets with higher levels of competition.

[47] The observation level of this test is firm-market-BTD announcement date. The sample includes rival and comparable control firms, the latter with projects in markets with similar competition levels. More details on the construction of the sample and the variables are provided in Online Appendix I.D.2. We thank Cameron Ellis for suggesting this test.

[48] Catch-up is uncertain even if resources are invested to innovate.

[49] We also find that the variable *Shock Exposure* is significantly and negatively associated with firm announcement returns around BTD events. That is, BTD awards are perceived negatively by rivals, and especially rivals that are highly exposed to the shocked market.

We next examine the role of time that drug projects spend in development (on average within a therapeutic market), as a moderator of the "treatment" effect. We define *Dev. Time*, as a continuous variable at the market level, equal to the (time-series) average amount of time drugs spend in all stages of project development, (then cross-sectionally) averaged across all drugs in a market. BTD drugs are expected to be approved faster (see Hermosilla 2022 as well as figure I.E.2 in online appendix I.E.1). This implies that rival projects in markets with lengthy average development times are placed at a substantial competitive disadvantage when their target market is hit by a BTD drug. In other words, the BTD drug will likely be approved much sooner, and will also likely have established a considerable competitive advantage before the rival project is approved. We rerun our main tests including *Dev. Time* and report the results In Panel B of Table 5. They indicate that rivals are less likely to develop shocked projects in markets with lengthy development times, particularly when the ex-ante competitiveness of that market is high.

Finally, we explore the possibility that rivals learn about the effectiveness of the technology used by a BTD designated drug, and allow that to moderate their reaction to a shock in their own market. Competitors often monitor the developments of each other, and quickly adopt radical innovations that could help improve operational efficiency or increase revenues.[50] BTD awards imply a technology breakthrough, since the designation is awarded to drugs that demonstrate substantial improvements over existing therapies. We examine whether rivals adopt an existing BTD drug's technology to aid in the development of their own BTD-shocked drug, and whether this affects the graduation rate from phase-II to phase-III.

Panel C of Table 5 investigates the development rates of projects that use a technology that was part of a previously-BTD-designated drug. The variable *BTD Technology* is an indicator defined at the drug

[50] For example, the effectiveness of mRNA technology in Covid-19 vaccines has led many firms to use mRNA technology in developing drugs that target other medical conditions. Bhat et al (2021) note its potential in protein replacement therapy and the treatment of genetic disorders.

level. It equals one if the focal project uses the same technology (i.e., target-based action) as that of other projects that were previously awarded a BTD in any market. Note that this technology and the BTD drug that it was part of, could have been developed by any firm in any therapeutic market. The results in Panel C indicate that rivals are significantly more likely to develop shocked phase-II projects when *BTD Technology* is equal to one, and especially if the competition level of the shocked market is ex-ante low.

In summary, we document several channels through which BTD shocks influence the graduation rates of rival phase-II projects. In ex-ante high competition markets, highly exposed rivals and rivals developing projects in markets with lengthy development times appear significantly less likely to develop their shocked phase-II projects. In addition, rivals appear to quickly adopt technology used by previous BTD-awarded drugs. These rivals use the BTD technology to develop projects in shocked markets with ex-ante lower levels of competition.

4.3. Shocked Rivals' Project Development Elsewhere

Shocked (by BTD) rivals have the option to reallocate their resources to other projects – and therefore markets – in their portfolio.[51] This is a key motive behind our study of project-level innovation responses. To better understand the full repertoire of rival responses, we offer two new lines of inquiry. The first focuses on rivals' existing phase-II projects that target unshocked markets. The second focuses on new drug investigation projects (discovery stage).

4.3.1. Rival Phase-II Development in Never-BTD-Shocked Markets

This section examines rivals' phase-II development rates for projects in markets that *never* experience BTD shocks. Here we exclude all control projects owned by control (never-shocked) firms, so that we only analyze the projects of active rivals (i.e., rivals that recently experienced a BTD shock in any of their markets) in never-shocked markets. The logic behind this empirical choice is to create a sample that allows us to examine whether development decisions vary by rival type. Since this sample includes

[51] We thank N. Prabhala for suggesting this line of inquiry.

only phase-II projects of active rivals but in markets that never experience BTD shocks, defining an indicator for BTD shocks is not possible at the drug or market levels (all markets and projects in this sample never experience BTD shocks). Instead, we need to define BTD shock indicators at the firm-level.[52]

We label two types of rivals based on the level of competition in the market where the rival experienced the BTD shock. The first (second) type includes rivals that were recently shocked in markets with ex-ante high (low) levels of competition; i.e. above (below) that of the sample median. We then rerun our main Cox Proportional hazards specification. We include an indicator, *Rival HiComp Shock* (that identifies the first type of rival), and equals one for rivals that were recently shocked in a more competitive market. We implicitly use the second type of rivals as the base group. We also define a variable, *Focal Mkt Comp*, that measures the level of competition in the (never-shocked) market *targeted* by the active rival's focal project. Note that *Rival HiComp Shock* is a firm-level measure based on the level of competition in a shocked market, whereas *Focal Mkt Comp* is a market-level measure based on the level of competition in the focal project's target market.

Table 6 presents results. They show a pattern similar to that in Table 4. Rivals that are shocked in an ex-ante high competition market are less likely to develop their projects in never-shocked markets that also show high levels of competition. Furthermore, rivals shocked in ex-ante high competition markets are more likely to develop projects targeting markets with lower levels of competition. Taken together, rivals shocked in high competition markets reshuffle their project portfolio away from more competitive markets and towards less competition markets, consistent with Aghion et al. (2005).

4.3.2. Drug Project Initiations of BTD Rivals

Shocked rivals may also eschew development of phase-II projects overall and instead dedicate resources to new discovery-stage drug investigations. These are known as drug project initiations. We

[52] For example, if a rival develops projects that target 2 markets: X and Y, and market X is shocked, then we would exclude all projects in market X, include only projects in market Y, and examine their development rates conditional on the targeted market's characteristics.

analyze their likelihood as a function of the shocked market competitiveness, as well as the new drug's target market competitiveness. Here we again restrict our focus to the sample of active rivals. We identify all quarters in which a rival experiences a BTD shock in any of its markets. Then we examine that rival's drug initiations in the subsequent 8 (or 4) quarters.

To capture the shocked market's competitiveness while recognizing that a firm may initiate in a different market, we again create the variable, *Rival HiComp Shock*. It equals one for rivals that were shocked in a highly competitive market in the last 8 (or 4) quarters, zero otherwise. The dependent variables are defined as follows: *IN* is a firm level indicator equal to one in quarters when a firm initiates a new drug project; *INLowComp (INHiComp*) is a firm level indicator equal to one in quarters when a firm initiates a new drug project in a low (high) competition market; *INBTDTech* is a firm level indicator equal to one in quarters when a rival initiates a new drug project that uses a technology that is similar to that used by a previously BTD-designated drug.

We run OLS regressions of each dependent variable on the *Rival HiComp Shock* variable. The observation level of the analysis sample is a firm-quarter. We include firm and calendar quarter fixed effects, along with standard errors clustered at the firm level. Table 7 presents the results. They indicate that rival firms who were recently shocked in more competitive markets are more likely to initiate new projects. This result is pronounced when the new markets show lower levels of competition. Furthermore, these rivals are also significantly more likely to initiate projects that use a technology of a previously BTD-awarded drug. Taken together with prior results, rivals shocked in markets with ex-ante high levels of competition generally shift their focus and resources to projects in markets with lower levels of competition. They are also more likely to develop projects that use a previously FDA-recognized superior technology.

4.4. Phase-II Graduation Rates, BTD Shock Events, and Ex-ante Market Levelness

Our empirical design hinges on BTDs as an unleveling shock to the therapeutic market. This is a

more defensible assumption if we can restrict our analysis to markets that are more demonstrably level ex-ante. We use this section to investigate the role of ex-ante market levelness on the effect of BTD shocks on development decisions.

Aghion et al. (2005) define ex-ante leveled markets (i.e. neck-and-neck markets) as those where incumbent firms are operating at similar technological levels. Since FDA approval to market a drug requires successful reviews at both the safety and efficacy levels, we identify markets in which all participating firms have FDA approved-for-sale drugs as "leveled". We also define a corresponding set of markets where none of the participating firms has an FDA approved-for-sale drug, as "leveled". We then rerun our main tests for these two subsamples, separately. It is worth emphasizing that the data-indicated competition levels within both types of ex-ante leveled markets are overwhelmingly low. This lends further support to our selection criteria. Aghion et al. (2005) predict that ex-ante leveled markets are mostly low competition markets in equilibrium.

We report our hazard results in Table 8. They indicate robustness of our main inference to the subsampling on strictly ex-ante leveled markets. Following a BTD's un-leveling of the market, shocked rivals accelerate development of their phase-II projects in markets with ex-ante lower levels of competition. The relationship is significantly weaker as market competitiveness rises (column 2). Two other points are noteworthy in Table 8. The results are particularly pronounced in panel B where we subsample on markets with no FDA approved-for-sale drugs. Arguably this is where a BTD event is huge news. Second, in panel D where we study the corollary subsample of ex-ante unleveled markets, we see the usual relationship continues to prevail. This suggests the BTD event is likely to further unlevel markets that were already unleveled; the model does not require strict leveling ex-ante to hold empirical water.

Finally, in untabulated tests we find similar results when we restrict our sample to phase-II projects in ex-ante leveled markets with only two active firms. In this case, one of the two firms receives a BTD award. Although this test involves a very small sample of about 36 markets, it leaves little room for

erroneous classification of market levelness, since the two competing firms owned projects in the same stage of development, and had identical competitive positions before one of the firms is granted a BTD.

4.5. A Firm-Level Analysis of Phase-II Development and BTD Shock Events: The Aggregation Problem

One of the key messages in this paper is that the conflicting findings in prior papers studying the competition – innovation relationship is likely due to an aggregation problem. The extant literature uses data aggregated to the firm-level or industry-level. As shown by Hoberg and Phillips (2021), firms often compete in multiple product markets with varying interests within each, and this scope-expansion has increased over time. Thus firm-level data may sometimes misidentify shocked rival firms if these firms are shocked in product markets that are not identified by the firm's primary industry classification. Moreover, firm-level data may not capture the importance of a shocked market to the firm – it may overweight or dilute the true extent of the shock to the firm. Firm-level measures of innovation suffer from similar issues. The R&D expense reported in firm financial statements does not identify the distribution of funds across markets, nor would it capture cases where a firm does not change the R&D expense levels but redistributes resources away from R&D in one product market and towards another.

We demonstrate the potential issues associated with the aggregation problem by replicating our baseline tests using a sample that aggregates the full phase-II sample to the firm level. We construct this aggregated firm-level data as follows: we aggregate the *Development Dummy* variable to the firm level such that it takes a value of one if, in quarter *t*, any of the firm's phase-II projects graduates to phase-III. We also aggregate the *BTD Shock* dummy to equal one if any of the firm's phase-II projects experiences a BTD shock in its target market. The competition measure is aggregated to the firm-level by computing the weighted average competition level across all markets that a firm has projects in during quarter t. Weights are assigned based on the number of a firm's projects in that market. We run an OLS regression using the aggregated Development Dummy as the dependent variable, and the aggregated BTD Shock variable and

Competition variables as the main regressors.[53]

Table 9 presents the results from this analysis. The results no longer show any statistically significant relationships between BTD shocks and phase-II development. Noteworthy is the positive sign on the coefficient in column 4, which had previously appeared negative and significant in all other tests. This highlights the significance of the noise and potential measurement errors introduced by aggregating project-level data up to the firm-level.

5. Robustness Tests

In this section, we examine the robustness of our main results. We first assess (and eventually dismiss) the possibility that firm innovation is driven by BTD-designation-chasing. We also replicate our main results using alternative samples. Finally, we examine the robustness of our main findings to alternative competition measures and therapeutic market definitions.

5.1. Designation Chasing Projects as Potential "False Negatives"

In a concurrent study, Hermosilla (2022) argues that the BTD program encouraged drug development in markets with high FDA attention (high policy exposure). The markets cover serious or life-threatening indications, and he shows that they experienced an increase in the flow of new therapies *after* a BTD in that market. Hermosilla (2022) concludes that such "designation chasing" lowered the average quality of these projects since the therapies would either obtain their own BTD or be quickly abandoned.

If our sample of rival phase-II projects is dominated by such attempts, this could drive the lower development hazards and imply our results have an alternative explanation. We address this alternative in two ways. First we subsample on phase-II projects that were already in existence (perhaps in an earlier

[53] Unlike our drug-level tests in Table 4, we are unable to run these tests using a hazard model because it would be challenging to define the analysis time (which previously was the number of quarters since the focal project started phase-II development) for firms with multiple projects. Moreover, a firm's observations would be dropped after the first development quarter (i.e., after the first success or survival incident).

phase) before the very first BTD in their market. In other words, these particular phase-II projects are unlikely to be designation-chasers. Second, we use Hermosilla's (2022) metric for BTD Policy Exposure as a blunt control by subsampling on those markets with low exposure.

For the first test (where we replicate our main tests using only the projects that were in place before the first shock entered the market), we offer results in Table 10. The findings are consistent with those of Table 4. BTD shocks in more (less) competitive markets lower (raise) the likelihood of continuation from phase-II to phase-III; even among these projects that are less subject to the concern about designation-chasing.

Our second test involves replicating our main analysis using subsamples partitioned on BTD *policy* exposure. We obtain BTD policy exposure data from Hermosilla (2022)[54] and match these to our phase-II sample. We drop projects in markets that do not match to the policy exposure data. We divide the sample into low and high policy exposure using 50% as the cutoff threshold.[55] We run our main Table 4 tests using these two subsamples and report the results in Table 11. If designation chasing projects are driving our results, then we would not expect to observe our main documented effect in the *low* policy exposure sample. The results suggest otherwise. BTD shocks have a negative (positive) impact on phase-II development rates in high (low) competition markets, even in the sub-sample where fewer projects are likely to chase the designation.

In summary, we find that our results are not driven by the potential systematic changes that affect a market after the first BTD shock. This provides evidence in favor of the exogeneity of the BTD events and confirms the robustness of our main findings.

5.2. Robustness Checks with Alternative Samples

We also replicate our main results using two alternative samples that control for systematic

[54] With deep gratitude expressed for sharing.

[55] BTD policy exposure is a continuous variable with values between zero and one. A value of one indicates that the market is very likely to experience a BTD award, and vice versa.

differences between eventually shocked markets and control markets. In the first alternative sample, we match each BTD-shocked project in the full phase-II sample to a single project from a pool of potential control projects. Control projects must satisfy the following criteria. At the drug-level, it must have started phase-II development within 5 years of the treated drug. At the market-level, it must target a market in the same quartile of competition as that of the treated drug. At the firm-market-level, the control firm's exposure to the control project's market must be in the same quartile as that of the treated firm's exposure to the treated project's market.[56] Finally, at the firm-level, the size of the control firm developing the control project must be in the same quartile as that of the treated firm developing the treated project. Size is measured as the total number of projects owned by the firm. We then randomly choose one control from the eligible set, to match with the treated project. The final sample consists of 2,399 phase-II projects that correspond to 36,416 unique project-quarter observations. It is noteworthy that the differences between the characteristics of the shocked and control projects are insignificant.

We replicate our main tests of Table 4 using the characteristics-based matching sample and report the results in Panel A of Table B1 in the main appendix B. The results are consistent in direction, but stronger in magnitude and statistical significance. This suggests that our main findings in Table 4 are not driven by systematic differences between shocked and control projects.

Another potential concern with our data is related to the distribution of BTD shocks across therapeutic markets. More specifically, about half the BTD designations in our sample are awarded to projects that target cancer markets. A critical reader may question whether our results are driven by unobservable factors specific to cancer markets. We therefore construct our second alternative sample by dropping all drug projects that target any of the cancer and neoplasms markets, from the full phase-II sample. Projects in these (excluded) markets are identified if the first letter of their assigned ICD-10 code

[56] Exposure is measured as the number of projects a firm develops in a market divided by the total number of projects developed by the same firm.

is “C.” The final sample consists of 3,224 phase-II projects that correspond to 38,572 unique project-quarter observations.

We rerun our main tests using this sample and report the results in Panel B of Table B1 in the main appendix B. Here too the results are consistent with our main findings, suggesting that our documented effect is not driven by market-specific factors.

5.3. Robustness Checks with Alternative Competition Measures

Competition plays a first-order role in our tests. This necessitates investigation into the robustness of our results using alternative measures of it. Ideally, competition would be calculated using sales-based measures, e.g., HHI index. Notwithstanding the limitations of such measures in pharma (as discussed in section 1.3), we do create one sales-based competition measure (HHI) and re-run our main analysis. Details on the construction of the HHI measure are provided in Online Appendix I.E section I.E.3. We also replicate our main results using the number of firms operating within a therapeutic market (instead of the number of projects in that market) to measure competitiveness. This latter measure of competition is also used in Cunningham et al (2021).

Table B2 in the main appendix B presents results from tests replicating our main Table 4 ones, but using the alternative competition measures. Panel A uses sales-based HHI to proxy market competitiveness, and Panel B uses the number of firms within a market as the competition measure. In both panels of Table B2, we find results consistent with our main findings. This suggests that our findings are not driven by the choice of proxy for market competitiveness.

5.4. Robustness Checks with Alternative Definitions for Therapeutic Markets

Another concern is that our results are driven by the choice of therapeutic market definition. Since we define therapeutic markets at the second subchapter of ICD-10, one may argue that this is too narrow. We address this concern by using two alternative definitions for therapeutic market: the more general

ICD-9 codes, and the first subchapter of the ICD-10 codes.[57] Panel A (Panel B) of Table B3 in the main appendix B replicates our main tests using therapeutic markets defined on the first subchapter of ICD-10 (ICD-9) codes. Again, our results support the robustness of our inferences and therefore indicate that they are not driven by the choice for market definition.

Taken together, the findings in this section help rule out alternative explanations for our results. They instead suggest that BTDs constitute a shock to the levelness within a product market, and firms respond to this shock based on the therapeutic market's ex-ante competitiveness.

6. Conclusions

We provide a novel test of the competition – innovation model in Aghion et al. (2005). Our setting is the pharma industry. This provides several benefits including highly innovation-oriented firms, granular product-market and project-investment data available for analysis, and time-varying cross-sectional shocks to specific product markets.

We specifically test the mechanism driving the theorized inverted-U relationship between competition and innovation. Shocks to product markets that exogenously unlevel them lead to firm innovative responses that vary by product market competitiveness. Our time-varying cross-sectional shocks are Breakthrough Therapy Designation (BTD) events on drug projects. These designations are determined by the FDA and signal the drug's expected superiority. This aligns with Aghion et al.'s characterization of unleveling events, and with the BTD recipient now considered a leader (while rivals become sudden laggards). Rivals respond by accelerating the progress of their drug projects in the shocked market when that market is less competitive. They decelerate the shocked project's development when the market is more competitive. The inverted-U receives causal empirical support.

[57] We again thank Manuel Hermosilla for generously providing us with the list of ICD-9 codes for medical indications in Cortellis.

We also explore drivers of rival responses to the shocks. Greater exposure to the shocked market discourages rival effort on their laggard drug, particularly when the drug resides in a more competitive market. Use of a BTD technology on the shocked drug project encourages development when the therapeutic market is less competitive.

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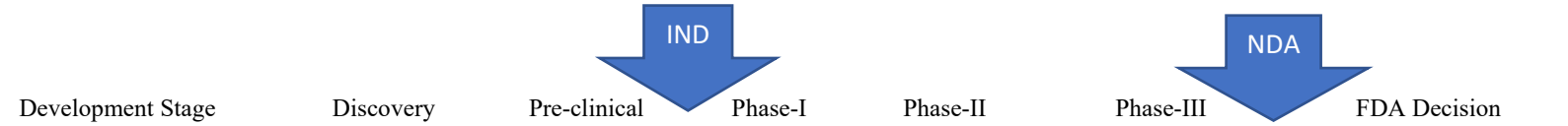
Figure 1: The Drug Development Process

This figure provides an illustrative description of the drug development process in the US. For each stage of development, the following information is provided. *EAP Application* identifies the recommended development stages for applying to any of the FDA's expedited approval programs. *Purpose* identifies the objective of each development stage. *# of participants* displays the average number of human volunteers in a given clinical stage. *Development time* reports the average number of years a drug project spends in a given stage before moving on to the next one. *Cost* provides the average cost (in $millions) associated with a given stage. *% move to next stage* reports the average percentage of drug projects in a given stage that eventually move on to the next one. *Approval Likelihood* shows the average probability that a drug project in a given stage eventually receives FDA approval. The two arrows in the first row indicate the timing for IND and NDA applications. IND is an abbreviation for investigational new drug application, and NDA is an abbreviation for new drug application.



Development Stage	Discovery	Pre-clinical	Phase-I	Phase-II	Phase-III	FDA Decision
EAP Application			*BTD*		*Fast Track*	*Accelerated Approval & Priority Review*
Purpose	Identify promising molecules	Animal and lab testing	Drug safety test in humans	Drug safety & efficacy tests in humans	Large-scale safety & efficacy tests in humans	
# of participants			10 to 50	50 to 200	200 to 3,000	FDA reviews evidence from clinical trials and approves or denies the NDA application
Development time	4 to 8 years		< 1 year	1 to 3 year	2 to 4 years	
Cost (in $ mil.)	1 to 7		1 to 5	7 to 20	10 to 75	
% move to next stage	30%		70%	33%	50%	
Approval likelihood	<5%		10%	15%	50%	

Figure 2: Time Trends in Phase-II Development Rates Around BTD Shocks

Each of the panels in this figure display coefficients from a Cox proportional hazards model that estimates the graduation (to phase-III) rates of rival phase-II projects relative to control projects, in the three years before, and three years after, BTD entry into a therapeutic market. The success event, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis time is the number of quarters since the start of phase-II. The analysis sample includes 5,194 phase-II projects, that were reportedly active at any point in time between 2010q1 and 2020q1. These projects were developed by 1,263 firms in 752 therapeutic markets (i.e., ICD-10 2nd subchapter codes). The final panel data consists of 62,033 unique project-quarter observations. The plotted coefficients are interaction variables between an indicator, *everBTDshocked*, which equals one if a phase-II project ever experiences BTD entry, with annual event time indicators for each of the 3 years before and after BTD entry. The bar caps cover the 95% confidence intervals for each coefficient. The Cox proportional hazards model is stratified by therapeutic market, includes calendar quarter fixed effects, and clusters standard errors by firm times market. The analysis sample in Figure 2A is the full sample of phase-II projects. The sample in panel B (panel C) includes phase-II projects in markets with low (high) competition, i.e., markets with competition levels in the bottom (top) median of all competition levels in the full phase-II sample.

Figure 2A: Full Sample

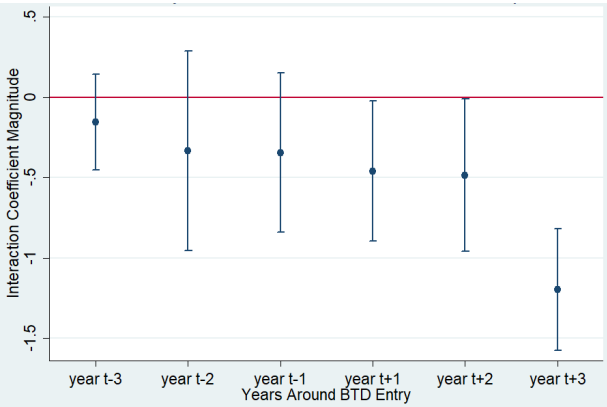


Figure 2B: Low Median of Competition Subsample

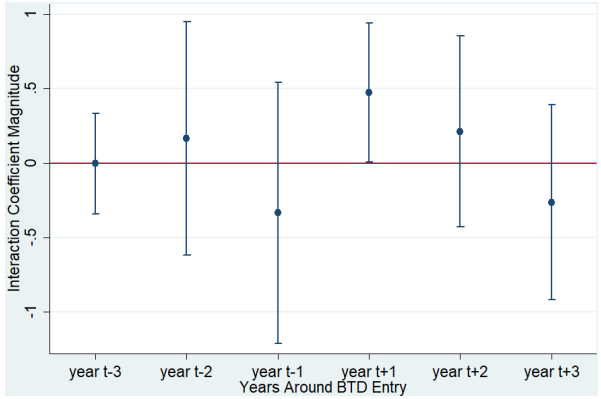


Figure 2C: High Median of Competition Subsample

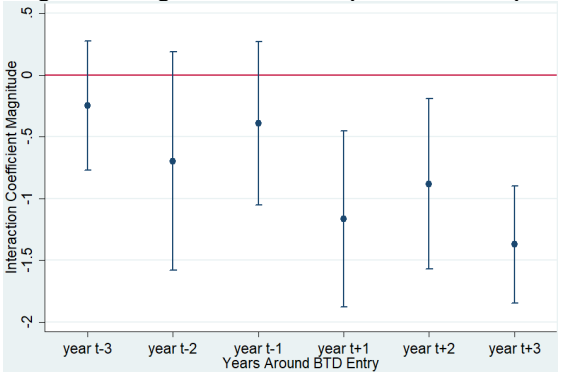


Table 1: Descriptive Statistics on BTD Events

This table presents descriptive statistics on the 253 unique BTD events in the sample. In columns 1 and 2, the distribution of these events is displayed by therapeutic markets, drug-projects, firms, firm public listing status (publicly traded or privately held), and firm product commercialization status (commercial or precommercial). Columns 3 and 4 provide the distribution of BTD events by order of market entry (first BTD to enter market or enters market after first BTD).

Variable	Count	Variable	Count
(1)	(2)	(3)	(4)
BTDs Granted	253	Number of First BTDs in Market	106
BTD Therapeutic Markets	145	Number of Subsequent BTDs in Market	167
BTD Drug Projects	272		
BTD Firms	113	BTDs Granted to Public Firms	221
Public BTD Firms	83	BTDs Granted to Private Firms	34
Private BTD Firms	30	BTDs Granted to Commercial Firms	180
Commercial BTD Firms	49	BTDs Granted to Precommercial Firms	80
Precommercial BTD firms	67	BTDs Granted to Public Commercial Firms	170
Public Commercial BTD Firms	42	BTDs Granted to Public Precommercial Firms	57
Public Precommercial BTD Firms	44	BTDs Granted to Private Commercial Firms	11
Private Commercial BTD Firms	7	BTDs Granted to Private Precommercial Firms	23
Private Precommercial BTD Firms	23		

Table 2: Stock Returns of BTD Firms, Rivals and Controls Around BTD Announcements

This table presents coefficients from OLS regressions of cumulative abnormal returns (CARs), around BTD announcement dates, on indicators that identify a firm's competitive status on the announcement date. The analysis sample includes 217 BTD announcement events and 693 firms, or 92,788 unique firm-BTD announcement date observations. The Full Sample, used in the first two columns, includes (up to) three firm types on any given announcement date: *BTD Firms*, who receive the BTD award; *Rivals*, who own projects in the same market where a competitor receives a BTD award; and *Control Firms*, who do not receive a BTD award nor own any projects in a BTD-shocked market. Firms in the full sample may be classified as BTD firms on some dates, and as rivals or controls on other dates. Calculation of the announcement returns is based on a market model with parameters estimated using the window of trading days [−271, −21], relative to the announcement date. The dependent variable (CAR) is actual return minus market-model-predicted return, cumulated over the three trading days [-1, +1] centered around the announcement. *Precommercial* is an indicator equal to one if the firm did not own any FDA approved-for-sale products as of the announcement date. Firm-announcement date observations are excluded if the firm had also experienced other important corporate events on the same day (e.g., CEO death). CARs are then winsorized at the 1% and 99% levels. Columns 3 and 4 present regression results for the sample of BTD firms and rivals, respectively. Fixed effects are indicated in the bottom two rows and standard errors are double clustered by firm and BTD announcement date. All firm-level variables are defined in Appendix A panel B. t-statistics are reported in parentheses. Statistical significance indicated as follows: *** p<0.01, ** p<0.05, * p<0.1

	Full Sample		BTD Firms Only	Rival Firms Only
	(1)	(2)	(3)	(4)
BTD Firm	0.016***	0.006**		
	(3.926)	(1.979)		
Rival	-0.002**	0.000		
	(-1.964)	(0.343)		
Precommercial		-0.000	0.033**	-0.004**
		(-0.005)	(2.027)	(-1.982)
BTD Firm * Precommercial		0.037***		
		(2.878)		
Rival * Precommercial		-0.005***		
		(-2.606)		
Observations	92,784	92,784	189	3,575
R-squared	0.085	0.085	0.100	0.117
Firm FE	Yes	Yes	No	No
Event Day FE	Yes	Yes	No	Yes

Table 3: Summary Statistics on the Phase-II Development Sample

This table presents summary statistics for phase-II projects, therapeutic markets, and developer firms appearing in the phase-II development sample. In all panels, statistics are displayed for the corresponding full sample (Full Sample in Column 1), the sample of rival phase-II projects that ever experienced a BTD shock (Ever BTD-Shocked in Column 2) and the sample of control phase-II projects that never experienced BTD entry (Never BTD-Shocked in Column 3). The variables *# of Phase-II Projects, # of Markets, # of Developing Firms* display the unique number of phase-II projects, number of therapeutic markets and number of firms developing phase-II projects in each corresponding sample, respectively. *% Graduated to Phase-III* reports the percentage of all phase-II projects that advance to phase-III in each corresponding sample. *Average Competition Level* displays the average level of competition in each sample. Competition is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. The observation level in the sample is project-quarter. Panel A uses the full sample of phase-II projects. The sample in panel B (panel C) includes phase-II projects in markets with low (high) competition, i.e., markets with competition levels in the bottom (top) median of all competition levels in the full phase-II sample. Drug-level variables are defined in Appendix A panel A.

	Full Sample	Ever BTD-Shocked	Never BTD-Shocked
	(1)	(2)	(3)
Panel A: Full Sample			
	(1)	(2)	(3)
# of Phase-II Projects	5,194	1,883	3,311
# of Markets	752	120	632
# of Developing Firms	1,263	564	699
% Graduated to Phase-III	0.934%	0.356%	1.270%
Average Competition Level	3.408	4.174	2.830
Number of Project-Quarter Obs.	62,033	22,749	39,284
Panel B: Low Competition Sample			
	(1)	(2)	(3)
# of Phase-II Projects	2,531	323	2,208
# of Markets	729	96	633
# of Developing Firms	856	192	664
% Graduated to Phase-III	1.224%	0.773%	1.298%
Average Competition Level	2.224	2.631	2.124
Number of Project-Quarter Obs.	31,040	4,397	26,643
Panel C: High Competition Sample			
	(1)	(2)	(3)
# of Phase-II Projects	2,683	1,562	1,121
# of Markets	127	53	74
# of Developing Firms	774	466	308
% Graduated to Phase-III	0.65%	0.256%	1.264%
Average Competition Level	4.594	4.698	4.413
Number of Project-Quarter Obs.	30,993	18,344	12,649

Table 4: BTD Events and Phase-II Graduation Rates

The tests in this table examine the effect of BTD shocks on the development likelihood of rivals' phase-II projects that reside in BTD shocked markets, relative to that of control (unshocked) projects. The table presents coefficients from the following regressions models: Cox Proportional Hazards (panel A); OLS (panel B); and binary logistic (panel C). The dependent variable (success event for the hazard model), *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis sample includes 5,194 phase-II projects, that were reportedly active at any point in time between 2010q1 and 2020q1. These projects were developed by 1,263 firms in 752 therapeutic markets (defined using ICD-10 2nd subchapter codes). The final panel data consists of 62,033 unique project-quarter observations. Phase-II projects owned by BTD-awarded firms are dropped from the sample if they target the same market in which the BTD firm was awarded. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the median level of competition in the full sample. All drug-level variables are defined in Appendix A panel A. asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

In panel A, the main Cox proportional-hazards specification is used, which stratifies the sample by market, clusters standard errors by firm times market and includes calendar year fixed effects. The analysis time is the number of quarters since the start of phase-II development. z-statistics are reported in parenthesis.

In panel B, coefficients are reported from OLS regressions with the following fixed effects: drug project, market, firm, calendar quarter, project vintage quarter and project age in quarters. Standard errors are double clustered by firm and market. Panel C reports results from using a logistic regression model with calendar year fixed effects and robust standard errors.

In both panels B and C, the sample is truncated in 2018q2 to account for the right-censoring bias, i.e., all phase-II projects started after 2018q2 are dropped from the sample. t-statistics are reported in parenthesis.

	Full Sample		Market Competition	
			Low	High
	(1)	(2)	(3)	(4)
Panel A: Cox Proportional Hazards Regression Model				
	(1)	(2)	(3)	(4)
BTD Shock	-0.318*	1.692***	0.626***	-0.544**
	(-1.773)	(3.571)	(2.611)	(-2.288)
BTD Shock*Competition		-0.499***		
		(-4.193)		
Observations	61,988	61,988	30,942	30,903
Panel B: OLS Regression Model				
	(1)	(2)	(3)	(4)
BTD Shock	-0.003*	0.023***	0.011**	-0.005**
	(-1.689)	(2.612)	(2.200)	(-2.025)
BTD Shock*Competition		-0.006***		
		(-3.230)		
Observations	58,001	58,001	29,646	28,343
Panel C: Binary Logistic Regression Model				
	(1)	(2)	(3)	(4)
BTD Shock	-0.564***	1.539***	0.377**	-0.886***
	(-4.275)	(4.268)	(2.018)	(-4.850)
BTD Shock*Competition		-0.519***		
		(-5.793)		
Observations	58,109	58,109	29,726	28,383

Table 5: The Mechanisms Behind BTD Rivals' Phase-II Development

The tests in this table explore the mechanisms by which rival firms respond to BTD shocks by adjusting their phase-II development. The table presents coefficients from the main Cox proportional-hazards specification, which stratifies the sample by market, clusters standard errors by firm times market and includes calendar year fixed effects. The analysis time is the number of quarters since the start of phase-II development. The success event of the hazard model, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis sample is the same one used (and described) in Table 4. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the median level of competition in the full sample. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

In panel A, the firm's exposure to a shocked market is examined. *Shock Exposure* is a variable defined at the firm-market level with values between zero and one, and is calculated as the percentage of a firm's total projects that reside in a BTD-shocked market in the same quarter of BTD entry.

Panel B examines the development likelihood of projects conditional on their average development times. *Dev. Time* is a continuous variable defined at the market level and measures the average development time within a market. It is calculated by first finding the average time to complete each stage within a market, then finding that market's overall average development time across all projects.

Panel C investigates the development rates of projects that use technology similar to that of a BTD designated drug. *BTD Technology* is an indicator defined at the drug level and is equal to one if the focal project uses the same target-based action (i.e., technology) as that of other projects that were previously awarded with a BTD in any market.

	Full Sample		Market Competition	
			Low	High
	(1)	(2)	(3)	(4)
Panel A: Firm Exposure to the Shock				
	(1)	(2)	(3)	(4)
BTD Shock	-0.518***	-0.212	0.539**	-0.278
	(-2.802)	(-1.057)	(2.103)	(-1.131)
Shock Exposure	0.124	0.292*	0.484**	0.157
	(0.761)	(1.695)	(2.243)	(0.593)
BTD Shock*Shock Exposure		-1.655***	-0.931	-1.812***
		(-3.135)	(-1.204)	(-2.605)
Observations	61,988	61,988	30,942	30,903
Panel B: Development in Markets with Lengthy Development Times				
	(1)	(2)	(3)	(4)
BTD Shock	-0.527***	0.038	0.834*	1.145
	(-2.869)	(0.069)	(1.670)	(1.396)
Dev. Time	0.040	0.045*	0.026	0.036
	(1.530)	(1.676)	(0.988)	(0.256)
BTD Shock*Dev. Time		-0.073	-0.058	-0.234**
		(-1.177)	(-1.020)	(-2.391)
Observations	60,563	60,563	29,570	30,993
Panel C: Phase-II Development of Projects with BTD Technology				
	(1)	(2)	(3)	(4)
BTD Shock	-0.561***	-0.890***	-0.185	-0.911***
	(-3.153)	(-4.196)	(-0.564)	(-3.255)
BTD Technology	0.171	-0.171	-0.083	0.017
	(1.129)	(-0.902)	(-0.302)	(0.058)
BTD Shock* BTD Technology		0.977***	1.145***	0.618
		(3.200)	(2.596)	(1.442)
Observations	61,988	61,988	30,942	30,903

Table 6: Rival Phase-II Development in Never-BTD-Shocked Markets

The tests in this table examine the effect of BTD shocks on the development rates of rival phase-II projects that reside in markets which never experienced BTD entry. The table presents coefficients from the main Cox proportional-hazards specification, which stratifies the sample by market, clusters standard errors by firm times market and includes calendar year fixed effects. The analysis time is the number of quarters since the start of phase-II development. The hazard success event, *Development*, is a drug level indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis sample focuses only on the phase-II projects of active rivals in never-shocked markets, and includes 1,939 phase-II projects, that were reportedly active at any point in time between 2012q4 and 2020q1. These projects were developed by 488 active rivals in 496 never-shocked therapeutic markets. The final panel data consists of 19,764 unique project-quarter observations. Firms become active rivals in the first quarter a BTD enters into a therapeutic market in which they operate, and remain active rivals until the end of the sample. *Rival HiComp Shock* is a firm level indicator equal to one starting from the first quarter when a rival experiences BTD entry into a high competition market (above the sample median competition level) in which the rival operates, and until the end of the sample period. When a rival experiences BTD entry in a low competition (below the sample median) market, the *Rival HiComp Shock* indicator is equal to zero. *Focal Mkt Comp* is calculated every quarter as the natural log of the total number of drug projects in the therapeutic market of the focal project. Note that the firm level indicator, *Rival HiComp Shock,* is based on the competition levels in the shocked market, whereas the market level variable, *Focal Mkt Comp,* is based on the competition levels in the never-shocked market of the focal project. Column 3 (column 4) reports results from using the sample of phase-II projects in never-shocked markets with competition levels below (above) the median level of competition in the sample. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

	Full Sample		Focal Mkt Competition	
			Low	High
	(1)	(2)	(3)	(4)
Rival HiComp Shock	-0.316	1.431**	0.598*	-0.757**
	(-1.501)	(1.987)	(1.796)	(-2.682)
Rival HiComp Shock*Focal Mkt Comp.		-0.505***		
		(-2.895)		
Observations	19,764	19,764	9,594	10,170

Table 7: Drug Project Initiations of BTD Rivals

The tests in this table investigate the effect of BTD shocks on the drug project initiations of rival firms. The table presents coefficients from OLS regressions with firm and calendar quarter fixed effects and with standard errors clustered at the firm level. The analysis sample includes only active rivals and the observational level is firm-quarter. Firms become active rivals in the first quarter when a BTD enters a therapeutic market in which they operate, and remain active rivals until the end of the sample period. There are 1,139 active rivals that were reportedly active at any point in time between 2012q4 and 2020q1. The final panel consists of 12,580 firm-quarter observations. The dependent variables are defined as follows: *IN* is a firm level indicator equal to one in quarters when a firm initiates a new drug project; *INLowComp (INHiComp*) is a firm level indicator equal to one in quarters when a firm initiates a new drug project in a low (high) competition market that falls below (above) the sample median competition level; *INBTDTech* is a firm level indicator equal to one in quarters when a rival initiates a new drug project that uses a technology that is similar to that used by a previously BTD designated drug. In the first four (last four) columns, *Rival HiComp Shock* is a firm level indicator equal to one in the first 8 (4) quarters after a rival experiences BTD entry into a high competition market (above the sample median competition level) in which the rival operates. Note that *Rival HiComp Shock* is based on competition levels in shocked markets, whereas both *INLowComp* and *INHiComp* are based on the competition levels in markets where the corresponding project initiation had occurred. All firm-level variables are defined in Appendix A panel B. t-statistics are reported in parenthesis. asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

	Shock Indicator Active for 8 Quarters After Shock				Shock Indicator Active for 4 Quarters After Shock			
Dependent Variable	IN	INLowComp	INHiComp	INBTDTech	IN	INLowComp	INHiComp	INBTDTech
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Rival HiComp Shock	0.025**	0.018**	0.009	0.014**	0.026**	0.016**	0.015	0.017**
	(2.284)	(2.415)	(0.868)	(2.296)	(2.400)	(1.978)	(1.519)	(2.565)
Constant	0.152***	0.073***	0.110***	0.026***	0.152***	0.074***	0.111***	0.026***
	(28.468)	(21.360)	(22.732)	(8.241)	(50.067)	(35.358)	(40.943)	(14.207)
Observations	12,561	12,561	12,561	12,561	12,561	12,561	12,561	12,561
R-squared	0.287	0.230	0.256	0.213	0.287	0.230	0.257	0.213

Table 8: Phase-II Development Around BTD Shocks and Ex-ante Market Levelness

The tests in this table examine the effect of BTD shocks on the development likelihood of phase-II projects conditional on the ex-ante levelness of the market. The table presents coefficients from the main Cox Proportional Hazards specification, which stratifies the sample by market, includes calendar year indicators and clusters standard errors by firm times market. The model's success event, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis time is the number of quarters since the start of phase-II development. The analysis sample in panels A, B and C (in panel D) include phase-II projects in ex-ante leveled (unleveled) markets that have ever experienced BTD entry and control projects that are also in ex-ante leveled (unleveled) markets that have never experienced a BTD event. Market ex-ante levelness (defined below) is measured in the quarter of BTD entry for shocked projects, and is measured for control projects in the quarter that centers a project's time series. The full sample of ex-ante leveled (unleveled) markets includes 2,834 (2,360) phase-II projects corresponding to 34,727 (27,306) unique project-quarter observations. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the full phase-II sample's median level of competition. The sample used in Panel A includes projects in ex-ante leveled markets where all participating firms own at least one approved-for -sale product. Whereas in Panel B, the sample includes projects in ex-ante leveled markets where none of the competing firms own an approved-for-sale product. In Panel C, the sample includes projects in both types of ex-ante leveled markets. The sample used in Panel D includes projects that reside in ex-ante unleveled market where at least one firm does not own an approved-for-sale product and at least one firm does. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as: *** p<0.01, ** p<0.05, * p<0.1

	Full Sample		Market Competition	
			Low	High
	(1)	(2)	(3)	(4)
Panel A: Ex-ante Leveled: All Firms Within the Market Own Approved-for-Sale Products				
	(1)	(2)	(3)	(4)
BTD Shock	1.280**	1.916**	1.423**	34.669***
	(2.157)	(1.964)	(2.466)	(32.086)
BTD Shock*Competition		-0.304		
		(-0.720)		
Observations	13,085	13,085	11,876	1,209
Panel B: Ex-ante Leveled: Markets with No Approved-for-Sale Products				
	(1)	(2)	(3)	(4)
BTD Shock	-0.039	3.869***	0.967***	0.471
	(-0.125)	(2.862)	(2.646)	(0.580)
BTD Shock*Competition		-1.032***		
		(-2.872)		
Observations	21,618	21,618	13,856	7,762
Panel C: Ex-ante Leveled: Markets in which Either All or None of Firms Own Approved-for-Sale Products				
	(1)	(2)	(3)	(4)
BTD Shock	0.362*	2.874***	0.820***	0.096
	(1.652)	(4.278)	(3.634)	(0.161)
BTD Shock*Competition		-0.768***		
		(-3.816)		
Observations	34,703	34,703	25,732	8,971
Panel D: Ex-ante Unleveled Markets				
	(1)	(2)	(3)	(4)
BTD Shock	-0.655***	2.906**	1.782*	-0.619***
	(-2.879)	(2.324)	(1.817)	(-3.811)
BTD Shock*Competition		-0.731***		
		(-2.798)		
Observations	27,286	27,286	5,141	14,128

Table 9: A Firm Level Analysis of Phase-II Development and BTD Shocks

The tests in this table examine the effect of BTD events on phase-II development using aggregated firm level data. The table presents coefficients from OLS regressions that include firm and calendar quarter fixed effects, and cluster standard errors by firm. The analysis sample includes 1,263 firms that developed at least one phase-II projects at any point in time between 2010q1 and 2020q1. The final panel consists of 19,459 unique firm-quarter observations. The dependent variable, *Firm Development*, is a firm level indicator equal to one in the quarter when any of a firm's phase-II projects graduate to phase-III, and equal to zero in all quarters when a firm's projects remain in phase-II. *Firm BTD shock* is a firm level indicator equal to one starting from the quarter in which any of a firm's targeted markets experience BTD entry and until the end of the sample. *Firm Competition* is a firm level variable that measures the aggregate level of competition a firm is facing. It is calculated every quarter by first finding the level of competition in each of a firm's targeted markets (as in Table 4), then computing a weighted average across all the markets of a firm, with weights assigned by the number of projects the firm owns in that market. All firm-level variables are defined in Appendix A panel B. t-statistics are reported in parenthesis. asterisks indicate statistical significance as: *** p<0.01, ** p<0.05, * p<0.1

	Full Sample		Firm Competition	
Sample			Low	High
	(1)	(2)	(3)	(4)
Firm BTD Shock	0.007	0.011	0.009	0.006
	(1.237)	(1.544)	(0.944)	(0.725)
Firm BTD Shock*Firm Competition		-0.005		
		(-1.455)		
Observations	19,434	19,434	9,700	9,702
R-squared	0.129	0.129	0.155	0.180

Table 10: BTD Events and Phase-II Development: Projects Initiated Before BTD Entry

The tests in this table are similar to those reported in Table 4, but with one difference: phase-II projects that are ever shocked are only included in the sample if they started phase-II development *before* the first BTD entered their market, i.e., the sample used here excludes projects that started phase-II development *after* the first BTD event had occurred. The table presents coefficients from the following regressions models: Cox Proportional Hazards (panel A); OLS (panel B); and binary logistic (panel C). The dependent variable (success event for the hazard model), *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis sample includes 3,987 phase-II projects, that were reportedly active at any point in time between 2010q1 and 2020q1. These projects were developed by 1,137 firms in 737 therapeutic markets (defined using ICD-10 2nd subchapter codes). The final panel data consists of 51,344 unique project-quarter observations. Phase-II projects owned by BTD-awarded firms are dropped from the sample if they target the same market in which the BTD firm was awarded. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the median level of competition in the full sample. All drug-level variables are defined in Appendix A panel A. asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

In panel A, the main Cox proportional-hazards specification is used, which stratifies the sample by market, clusters standard errors by firm times market and includes calendar year fixed effects. The analysis time is the number of quarters since the start of phase-II development. z-statistics are reported in parenthesis.

In panel B, coefficients are reported from OLS regressions with the following fixed effects: drug project, market, firm, calendar quarter, and project vintage and age. Standard errors are double clustered by firm and market. Panel C reports results from using a logistic regression model with calendar year fixed effects and robust standard errors.

In both panels B and C, the sample is truncated in 2018q2 to account for the right-censoring bias, i.e., all phase-II projects started after 2018q2 are dropped from the sample. t-statistics are reported in parenthesis.

	Full Sample		Market Competition	
			Low	High
	(1)	(2)	(3)	(4)
Panel A: Cox Proportional Hazards Regression Model				
	(1)	(2)	(3)	(4)
BTD Shock	-0.318*	1.546**	0.573**	-0.594**
	(-1.718)	(2.473)	(2.052)	(-2.069)
BTD Shock*Competition		-0.469***		
		(-2.877)		
Observations	51,309	51,309	29,905	21,290
Panel B: OLS Regression Model				
	(1)	(2)	(3)	(4)
BTD Shock	-0.004*	0.021**	0.011**	-0.005**
	(-1.760)	(2.128)	(2.196)	(-2.015)
BTD Shock*Competition		-0.006***		
		(-2.774)		
Observations	48,132	48,043	28,584	19,459
Panel C: Binary Logistic Regression Model				
	(1)	(2)	(3)	(4)
BTD Shock	-0.485**	1.241**	0.448**	-1.066***
	(-2.523)	(2.361)	(1.980)	(-3.655)
BTD Shock*Competition		-0.428***		
		(-3.291)		
Observations	49,136	49,136	28,797	20,328

Table 11: Phase-II Development, BTD Shocks and Policy Exposure.

The tests in this table examine the effect of BTD shocks on the development likelihood of phase-II projects conditional on the extent the target market is exposed to BTD policy. The table presents coefficients from the main Cox proportional-hazards specification, which stratifies the sample by market, clusters standard errors by firm times market and includes calendar year fixed effects. The analysis time is the number of quarters since the start of phase-II development, and the success event, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. *Policy Exposure*, introduced by Hermosilla (2022), is a variable with values between zero and one that measures the extent to which the FDA considers a medical condition (i.e., therapeutic market) serious or life-threatening. It is essentially a market-level measure of the likelihood that a BTD designation is granted within a market. The analysis sample is constructed by matching the full phase-II sample to policy exposure data, then dividing the sample into subsamples conditional on the extent of policy exposure. In the first four columns (last four columns), results are reported from analyses that use the subsample of phase-II projects in markets with low (high) policy exposure less than or equal to (greater than) 50%. The final low policy exposure (high policy exposure) sample consists of 2,001 (1,840) phase-II that correspond to 24,089 (21,208) unique project-quarter observations. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. Columns 3 and 7 (columns 4 and 8) reports results from using the sample of phase-II projects in markets with competition levels below (above) the median level of competition in the full sample. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

	Low Policy Exposure				**High Policy Exposure**			
	Full Low Policy Exposure Sample		Market Competition		Full High Policy Exposure Sample		Market Competition	
			Low	High			Low	High
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
BTD Shock	0.047	2.388***	0.705**	-1.034*	-0.688***	2.641***	0.588	-0.737***
	(0.171)	(3.055)	(2.129)	(-1.750)	(-3.086)	(2.798)	(1.357)	(-2.643)
BTD Shock*Competition		-0.693***				-0.721***		
		(-2.998)				(-3.372)		
Observations	24,067	24,067	15,955	8,112	21,196	21,196	6,753	14,443

Appendix A: Variable Definitions

Table A1: Drug-level, market-level and firm-level variable definitions

Panel A: Drug-level Variables

Variable	Definition
BTD Shock	an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters.
BTD Technology	an indicator defined at the drug level and is equal to one if the focal project uses the same target-based action (i.e., technology) as that of other projects that were previously awarded with a BTD in any market.
Development	an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II.

Panel B: Market-level and Firm-Market-Level Variables

Variable	Definition
Competition	Calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. The count includes approved products and projects in any stage of development.
Development Time	A continuous variable defined at the market level and measures the average development time within a market. It is calculated by first finding the average time to complete each stage within a market, then finding that market's overall average development time across all stages.
Ex-ante Leveled Markets	Markets in which all participating firms have similar development statuses There are two types. In the first, all participating firms own at least one approved-for -sale product. Whereas in second, none of the competing firms own an approved-for-sale product, i.e., markets without any approved products.
Ex-ante Unleveled Markets	Markets where at least one of the participating firms does not own an approved-for-sale product and at least one firm does.
Focal Mkt Competition	The competition level in the market targeted by the focal drug project. Competition is defined above.
Policy Exposure	introduced by Hermosilla (2022), is a variable with values between zero and one that measures the extent to which the FDA considers a medical condition (i.e., therapeutic market) serious or life-threatening. It is essentially a market-level measure of the likelihood that a BTD designation is granted within a market.
Shock Exposure	The number of projects a firm develops in a market divided by the total number of projects developed by the same firm.

Panel C: Firm-level Variables

Variable	Definition
BTD Firm	A dummy variable equal to one if the firm receives a BTD designation for one of its drugs on a given date, and zero otherwise.
Firm BTD Shock	a firm level indicator equal to one starting from the quarter in which any of a firm's targeted markets experience BTD entry and until the end of the sample.
Firm Competition	The weighted-average of the drug-level variable "Competition" across all the ICD-10 markets that a firm is active in, in a given quarter. Weights are assigned by the number of projects in each ICD-10 market.
IN	indicator equal to one in quarters when a firm initiates a new drug project
INLowComp	a firm level indicator equal to one in quarters when a firm initiates a new drug project in a low competition market that falls below the sample median competition level.
INHiComp	a firm level indicator equal to one in quarters when a firm initiates a new drug project in a high competition market that falls above the sample median competition level.
INBTDTech	a firm level indicator equal to one in quarters when a rival initiates a new drug project that uses a technology that is similar to that used by a previously BTD designated drug.
Precommercial	an indicator equal to one if the firm did not own any FDA approved-for-sale products as of quarter *t*.
Rival	A dummy variable equal to one if the firm operates in a therapeutic market where BTD designation was awarded, and the firm did not receive the award, and zero otherwise.
Rival HiComp Shock	a firm level indicator equal to one in the first 8 (or 4) quarters after a rival experiences BTD entry into a high competition market (above the sample median competition level) in which the rival operates. Note that *Rival HiComp Shock* is based on competition levels in shocked markets

Appendix B: Additional Robustness Tests

Table B1: Robustness of the Phase-II Development Baseline Tests with Alternative Samples

The tests in this table replicate the baseline BTD events and phase-II development tests in Table 4, only using alternative samples. The table presents coefficients from the main Cox Proportional Hazards specification, which stratifies the sample by market, includes calendar year indicators and clusters standard errors by firm times market. The model's success event, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis time is the number of quarters since the start of phase-II development. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the full phase-II sample's median level of competition. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as: *** p<0.01, ** p<0.05, * p<0.1

In Panel A, the analysis sample is constructed by randomly matching each ever-BTD-shocked project (treated project) in the full phase-II sample to a single project from a pool of potential control projects. Control projects must satisfy the following criteria. First, at the drug-level, a control must have started phase-II development within 5 years of the treated drug. Second, at the market-level, a control must target a market in the same quartile of competition as that of the treated drug. Third, at the firm-market-level, the control firm's exposure to the control project's market must be in the same quartile as that of the treated firm's exposure to the treated project's market. Exposure is measured as the number of projects a firm develops in a market divided by the total number of projects developed by the same firm. Finally, at the firm-level, the size of the control firm developing the control project must be in the same quartile as that of the treated firm developing the treated project. Size is measured as the total number of projects owned by the firm. The final sample consists of 2,399 phase-II projects that correspond to 36,416 unique project-quarter observations.

In Panel B, the analysis sample is constructed by dropping all drug projects that target any of the cancer and neoplasms markets from the full phase-II sample. Projects in these (excluded) markets are identified if the first letter of their assigned ICD-10 code is "C." The final sample consists of 3,224 phase-II projects that correspond to 38.572 unique project-quarter observations.

	Full Sample		Market Competition	
			Low	High
	(1)	(2)	(3)	(4)
Panel A: Characteristic-Based Matching Sample				
	(1)	(2)	(3)	(4)
BTD Shock	-0.475***	4.017***	0.711**	-1.992***
	(-2.595)	(2.794)	(2.335)	(-5.033)
BTD Shock*Competition		-0.977***		
		(-3.218)		
Observations	36,386	36,386	18,240	18,146
Panel B: Excluding Cancer Therapeutic Markets				
	(1)	(2)	(3)	(4)
BTD Shock	-0.279	2.643***	0.795**	-0.962***
	(-1.241)	(5.083)	(2.394)	(-5.567)
BTD Shock*Competition		-0.792***		
		(-6.130)		
Observations	38,451	38,451	19,245	19,206

Table B2: Robustness of the Phase-II Development Baseline Tests with Alternative Competition Measures

The tests in this table replicate the baseline BTD events and phase-II development tests in Table 4, only using alternative samples. The table presents coefficients from the main Cox Proportional Hazards specification, which stratifies the sample by market, includes calendar year indicators and clusters standard errors by firm times market. The model's success event, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis time is the number of quarters since the start of phase-II development. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the full phase-II sample's median level of competition. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as: *** p<0.01, ** p<0.05, * p<0.1

In Panel A, the analysis sample is constructed by randomly matching each ever-BTD-shocked project (treated project) in the full phase-II sample to a single project from a pool of potential control projects. Control projects must satisfy the following criteria. First, at the drug-level, a control must have started phase-II development within 5 years of the treated drug. Second, at the market-level, a control must target a market in the same quartile of competition as that of the treated drug. Third, at the firm-market-level, the control firm's exposure to the control project's market must be in the same quartile as that of the treated firm's exposure to the treated project's market. Exposure is measured as the number of projects a firm develops in a market divided by the total number of projects developed by the same firm. Finally, at the firm-level, the size of the control firm developing the control project must be in the same quartile as that of the treated firm developing the treated project. Size is measured as the total number of projects owned by the firm. The final sample consists of 2,399 phase-II projects that correspond to 36,416 unique project-quarter observations.

In Panel B, the analysis sample is constructed by dropping all drug projects that target any of the cancer and neoplasms markets from the full phase-II sample. Projects in these (excluded) markets are identified if the first letter of their assigned ICD-10 code is "C." The final sample consists of 3,224 phase-II projects that correspond to 38.572 unique project-quarter observations.

	Full Sample		Market Competition	
			Low	High
	(1)	(2)	(3)	(4)
Panel A: HHI Competition Measure				
	(1)	(2)	(3)	(4)
BTD Shock	-0.513***	-1.416***	-0.244	-0.774***
	(-3.112)	(-4.243)	(-0.644)	(-3.442)
BTD Shock*HHI		2.663***		
		(3.243)		
Observations	56,732	56,732	25,927	30,081
Panel B: Number of Firms in Mkt Competition Measure				
	(1)	(2)	(3)	(4)
BTD Shock	-0.279*	2.703***	0.609***	-0.167*
	(-1.961)	(5.403)	(2.466)	(-1.807)
BTD Shock*Competition		-0.809***		
		(-6.291)		
Observations	61,845	61,845	30,921	30,924

Table B3: Robustness of the Phase-II Development Baseline Tests with Alternative Definitions for Therapeutic Market

The tests in this table replicate the baseline BTD events and phase-II development tests in Table 4, only using alternative samples. The table presents coefficients from the main Cox Proportional Hazards specification, which stratifies the sample by market, includes calendar year indicators and clusters standard errors by firm times market. The model's success event, *Development*, is an indicator equal to one in the quarter that a project graduates to phase-III, and equal to zero in all quarters where it remains in phase-II. The analysis time is the number of quarters since the start of phase-II development. *BTD Shock* is an indicator equal to one for all phase-II projects that reside in a BTD-shocked market in all quarters starting from the BTD shock quarter and until the end of the sample, and equal to zero for projects that were either never shocked by BTD entry, or eventually shocked but in the quarters before a BTD enters. *Competition* is calculated each quarter as the natural log of the total number of drug projects in a therapeutic market. In all panels, column 3 (column 4) reports results from using the sample of phase-II projects in markets with competition levels below (above) the full phase-II sample's median level of competition. All drug-level variables are defined in Appendix A panel A. z-statistics are reported in parenthesis. asterisks indicate statistical significance as: *** p<0.01, ** p<0.05, * p<0.1

In Panel A, the analysis sample is constructed by randomly matching each ever-BTD-shocked project (treated project) in the full phase-II sample to a single project from a pool of potential control projects. Control projects must satisfy the following criteria. First, at the drug-level, a control must have started phase-II development within 5 years of the treated drug. Second, at the market-level, a control must target a market in the same quartile of competition as that of the treated drug. Third, at the firm-market-level, the control firm's exposure to the control project's market must be in the same quartile as that of the treated firm's exposure to the treated project's market. Exposure is measured as the number of projects a firm develops in a market divided by the total number of projects developed by the same firm. Finally, at the firm-level, the size of the control firm developing the control project must be in the same quartile as that of the treated firm developing the treated project. Size is measured as the total number of projects owned by the firm. The final sample consists of 2,399 phase-II projects that correspond to 36,416 unique project-quarter observations.

In Panel B, the analysis sample is constructed by dropping all drug projects that target any of the cancer and neoplasms markets from the full phase-II sample. Projects in these (excluded) markets are identified if the first letter of their assigned ICD-10 code is "C." The final sample consists of 3,224 phase-II projects that correspond to 38.572 unique project-quarter observations.

	Full Sample		Market Competition	
			Low	High
Panel A: Therapeutic Markets Defined Using ICD-10 1st Subchapter Codes				
	(1)	(2)	(3)	(4)
BTD Shock	-0.418***	0.704**	0.310**	-0.474**
	(-3.840)	(2.518)	(1.962)	(-2.544)
BTD Shock*Competition		-0.291***		
		(-3.749)		
Observations	61,845	61,845	30,929	30,916
Panel B: Therapeutic Markets Defined Using ICD-9 Codes				
	(1)	(2)	(3)	(4)
BTD Shock	-0.505***	2.361***	0.093	-0.490**
	(-3.572)	(3.044)	(0.390)	(-2.294)
BTD Shock*Competition		-0.568***		
		(-3.591)		
Observations	60,102	60,102	30,044	30,058

Online Appendix for "Competition and Innovation Revisited: A Project-Level View"

The online appendix is structured as follows:

- Appendix I.A: ICD-10 Therapeutic Markets: Background and Description
- Appendix I.B: A Description of the Cortellis Database and the Processing Procedure
- Appendix I.C: Identifying BTD Designation Events
- Appendix I.D: Supplementary Results for the BTD Grant Announcement Returns Tests
- Appendix I.E: Supplementary Results for the Phase-II Development Tests
- References in the Online Appendix

Appendix I.A: Description of ICD-10 Markets

In Section I.A.1 of this appendix, we discuss the reasoning behind our choice to define therapeutic markets using 2nd subchapter ICD-10 codes. Next, we provide a general description of these markets in Table I.A.1 in Section I.A.2.

Section I.A.1: A Discussion on the Advantages of using 2nd Subchapter ICD-10 Codes to Define Therapeutic Markets

In our main tests, we define therapeutic markets using ICD-10 codes defined at the second subchapter (herein 2SC-ICD-10)[1]. We believe these (2SC-ICD-10) codes offer several advantages relative to other therapeutic market definitions (e.g., 1st subchapter ICD-10 (1SC-ICD-10) codes and ICD-9 codes). First, our objective is to identify rivals who operate in the same market where a BTD was awarded. It is therefore critical to ensure that these rival drug projects are substitutes of the BTD drug. 2SC-ICD-10 codes allow for the identification of rival projects that address the same exact indication. Whereas 1SC-ICD-10 codes and ICD-9 codes lump together a group of similar markets, with potentially different characteristics. For example, while myeloid leukemia (2SC-ICD-10 is "C92-0") is a very common type of cancer among adults and is therefore a very competitive indication, few drugs under development address the rare subtype promyelocytic leukemia (2SC-ICD-10 of "C92-4"). Both myeloid and promyelocytic leukemias have the same 1SC-ICD-10 ("C92") and ICD-9 code ("205"). Moreover, the FDA approves drugs for specific indications. This means that a drug cannot be prescribed for both types of leukemia unless it successfully completes separate clinical trials, and obtains FDA approval for each indication[2]. In addition, we find, in untabulated results, that the announcement returns of rivals around BTD announcements were significantly more negative when therapeutic markets were defined on 2SC-ICD-10 codes, relative to markets defined

[1] If an indication only has an ICD-10 code at the first subchapter level, (e.g., essential hypertension has an ICD-10 code of I10), we use the first subchapter designation (rather than deleting observations). We also find that our results hold similarly if we instead delete such indications.

[2] Drugs can be prescribed "off-label" without FDA approval, however, with the exception of rare case, the best available treatments for an indication are always drugs approved for that indication. Furthermore, firms with effective off-label treatments for an indication risk forgoing significant revenues because off-label uses are less known and many physicians avoid prescribing off-label therapies due to potential litigation risk.

on either of 1SC-ICD-10 or ICD-9 codes, suggesting that 2SC-ICD-10 codes may be identifying substitutes more accurately. Second, while 1SC-ICD-10 codes can vary on some dimensions (as illustrated in the leukemia example above), they also share many characteristics, e.g., subtypes of the same general disease, target the same organ or cells, use similar target-based actions to cure the condition, cause similar symptoms…etc. This motivates our decision to stratify the sample in the main (phase-II development) Cox proportional hazard tests by 1SC-ICD-10 codes. Doing so allows us to make "apples to apples" comparisons[3] [4]. As a reminder, the sample in our main tests defines therapeutic markets, rivals and BTD events using 2SC-ICD-10 codes. That is, the treatment effect is based on 2SC-ICD-10 codes, while the counterfactuals are based on 1SC-ICD-10 codes.

[3] For example, Lymphoma (2SC-ICD-10 is "C85-0") has 3 other variations: high grade b-cell lymphoma (2SC-ICD10 is "C85-10"); primary mediastinal large b-cell lymphoma (2SC-ICD-10 is "C85-20"); non-hodgkins lymphoma (2SC-ICD-10 is "C85-9"). Of these, only the last two experience BTD entry. This allows the treatment effect to be estimated relative to comparable counterfactuals (i.e., phase-II projects in the first two (never-shocked) markets) of the same age, stage of development, and with similar market characteristics.

[4] In Table B.3 of main Appendix B, we successfully replicate our baseline tests using therapeutic markets defined on 1SC-ICD-10 and ICD-9 codes.

Section I.A.2: Description of the ICD-10 Therapeutic Markets

Table I.A.1: Description of ICD-10 markets.

This table provides information on the medical conditions in each broad ICD-10 category. 1SC-ICD-10 codes that address a common medical condition are grouped together in each row. Source: "International Classification of Diseases 10th Revision". World Health Organization.

ICD-10 Market Code	ICD-10 Market Code Description
A00–B99	Certain infectious and parasitic diseases
C00–D48	Neoplasms
D50–D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
E00–E90	Endocrine, nutritional and metabolic diseases
F00–F99	Mental and behavioral disorders
G00–G99	Diseases of the nervous system
H00–H59	Diseases of the eye and adnexa
H60–H95	Diseases of the ear and mastoid process
I00–I99	Diseases of the circulatory system
J00–J99	Diseases of the respiratory system
K00–K93	Diseases of the digestive system
L00–L99	Diseases of the skin and subcutaneous tissue
M00–M99	Diseases of the musculoskeletal system and connective tissue
N00–N99	Diseases of the genitourinary system
O00–O99	Pregnancy, childbirth and the puerperium
P00–P96	Certain conditions originating in the perinatal period
Q00–Q99	Congenital malformations, deformations and chromosomal abnormalities
R00–R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
S00–T98	Injury, poisoning and certain other consequences of external causes
V01–Y98	External causes of morbidity and mortality
Z00–Z99	Factors influencing health status and contact with health services

Appendix I.B: A Description of the Cortellis Drug Development Database and the Processing Procedure

Table I.B.1 of Section I.B.1 provides an example of the drug development information included in the Cortellis database. Section I.B.2 describes the procedure used to identify the drug developing firms.

Section I.B.1: An Example of Drug Development History in Cortellis

Table I.B.1: An Example of Drug Development History in Cortellis

This table provides an example of the development milestone information listed in Cortellis. Target Actions, i.e., a drug's technology, is the molecule in the body upon which a drug performs its function. Extract provides a summary on a drug's ownership status, target markets and technology. DevelopmentStatusCurrent presents the most recent development on the drug-indication pairing. DevelopmentStatusHistory lists all previous developments for a drug-indication.

Drug Name	Originator	Active Companies	Target Actions	Inactive Companies	Extract	DevelopmentStatusCurrent	DevelopmentStatusHistory
IDE-196	Novartis	IDEAYA Biosciences	Protein kinase inhibitor	Novartis	IDEAYA Biosciences under license from Novartis Pharmaceuticals is developing IDE-196 (previously LXS-196; NVP-LXS-196), an oral immediate release tablet formulation, a protein kinase C inhibitor, for the potential treatment of metastatic uveal melanoma (MUM), solid tumors including, cutaneous melanoma, and colorectal cancer.	IDEAYA Biosciences Inc: US: Phase 2 Clinical: Colorectal tumor: 25-Jun-2019 IDEAYA Biosciences Inc: US: Phase 2 Clinical: Solid tumor: 25-Jun-2019 Novartis Pharmaceuticals Corp: US: Outlicensed: Uveal melanoma: 23-Oct-2018 IDEAYA Biosciences Inc: US: Phase 2 Clinical: Uveal melanoma: 25-Jun-2019 IDEAYA Biosciences Inc: US: Phase 2 Clinical: Melanoma: 25-Jun-2019	Novartis Pharmaceuticals Corp: US: Discovery: Uveal melanoma: 06-Nov-2015 Novartis Pharmaceuticals Corp: US: Phase 1 Clinical: Uveal melanoma: 01-Feb-2016 IDEAYA Biosciences Inc: US: Preclinical: Colorectal tumor: 23-Oct-2018 IDEAYA Biosciences Inc: US: Preclinical: Melanoma: 23-Oct-2018 IDEAYA Biosciences Inc: US: Preclinical: Solid tumor: 23-Oct-2018 IDEAYA Biosciences Inc: US: Phase 1 Clinical: Uveal melanoma: 23-Oct-2018

Section I.B.2: Identifying Drug Developing Firms in the Cortellis Database

Cortellis provides information the following for a drug: drug names, target therapeutic market, originating firm, current and previous owners, sales in 2018, technology, regulatory designations (e.g. breakthrough designation and priority review designation), patent status, and (most importantly) detailed history of key development milestones and dates.

Coretllis Data lists the originator firm for each drug. It also lists firms that are actively developing the drug, and (inactive) firms who had previously developed the drug. In addition, the "Extract" field contains elaborate information on the ownership of the drug, and whether the originating firm was acquired, is a subsidiary of another firm, was spun-off by another firm, or whether the firm changed its name. However, it does not always list the dates on which a drug's ownership changed.

We use several resources to identify the correct owner(s) of a drug in different on a given date. We obtain merger deal records from SDC platinum. We retrieve all merger deals occurring between January 2000 to December 2019 with targets in the biopharmaceutical industry. We also use the publicly available Informa's Scrip website, and google searches to identify firms and their owners.

Our matching strategy is similar in spirit to that of Cunningham et al (2021):

1. We use the comp_stnd package in Stata (Wasi and Flaeen (2013)) to standardize company names in both Cortellis and SDC. We further clean company names from European entity types (e.g., SAS, AB, NV…etc.), and from the words "Pharmaceuticals, Pharmaceutical, and Pharma."
2. We match firms listed Cortellis's Active Company- and Inactive Company fields to SDC merger deals using acquirer and target firm names, and retain only exact matches. We manually check all matches to ensure validity.
3. Using the list of Cortellis firms matched to SDC, we examine Cortellis's Extract field to identify patterns in the word descriptions of firms that change ownership. We identify several patterns, e.g. (XX, a subsidiary of YY), (XX, now YY), (XX, after its acquisition of YY), (XX, after its merger with YY) …etc. We use these patterns to flag other firms that had changed ownership.
4. We match these flagged Cortellis firms to SDC merger data using a fuzzy (non-exact) match. We manually check each match to ensure accuracy.
5. For flagged firms that did not match (or incorrectly matched) to SDC using the fuzzy matching method, we manually search Scrip and Google to identify if any changes in ownership had occurred.

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Appendix I.C: Identifying BTD Designations

Section I.C.1 of this appendix provides details on the procedure used to identify BTD designations. Figure I.C.1 of Section 1.C.2 presents an illustrative summary of the distribution of BTD events by year and therapeutic market. Section I.C.3 provides a discussion on the perception of BTDs as viewed by physicians, patients and the biopharmaceutical industry in general. Finally, Section I.C.4 discusses the results from tests that demonstrate the higher likelihood of approval for BTD drugs.

Section I.C.1: Identifying BTD Designation Events

We identify BTD events and match each to the corresponding firm, drug and indication as follows:

1. We utilize three resources to identify BTD awards. First, the "Regulatory Designation" field in Cortellis indicates whether a drug was awarded with a BTD, however, it does not identify the grant date, nor the designated indication[5]. Second, we use the Friends of Cancer Research (FOCR) website,[6]which identifies the BTD drug's name, the grant announcement date, the sponsoring firm and the designated indication(s). Finally, when possible, we also the financial statements[7] of a firm to verify the accuracy of our matches.
2. Cortellis provides two variables that identify the drug name – 1) Drug Name, and 2) Other Drug Names. The first variable usually identifies the active ingredient of a drug (generic name), and the second identifies all names given to a drug by any of its current, or previous, developers. We match the Cortellis data to the FOCR data on exact drug names. Unmatched drugs are processed in step 3 below. Matched drugs are manually verified.
3. For the sample of unmatched drugs (from step 2), we conduct a fuzzy (non-exact) match between Cortellis and FOCR using drug names, and manually verify the matched records.
4. For unmatched drugs identified by Cortellis as BTD-recipients but not included in FOCR, we search firm financial statements, FDA documents, and business media articles to find the grant date, developing firm and designated indication.
5. We investigate the cases where a BTD drug in FOCR did not match to Cortellis. We find 42 such drugs that either don't exist in Cortellis, or do exist but the designated indication does not.
6. Finally, we also verify our matches with the 143 BTDs reported in the online supplementary appendix for Hoffman et al. (2019).

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[5] As a reminder, a single drug may be developed for several indications. BTD designations are awarded to a drug-indication pairing. This implies that a BTD drug may be designated for some indications, but not for others. Cortellis identifies the BTD awards at the drug-level, and does not indicate the designated indication.

[6] https://www.focr.org/breakthrough-therapies

[7] For publicly listed BTD firms.

Section I.C.2: Distribution of BTD Awards by Year and Therapeutic Market

Figure I.C.1: Distribution of BTD grants by year, ICD-10 market and firm

This figure presents illustrative descriptions of the BTD awards in our sample. Figure I.C.1.A displays the distribution of BTD awards by year. Figure I.C.1.B displays this distribution by the therapeutic market in which a BTD was granted. These markets are defined using the first letter of their ICD-10 code. Refer to Table I.A.1 in Online Appendix I.A for the definitions of the ICD-10 markets.

Figure I.C.1.A: Distribution by Year

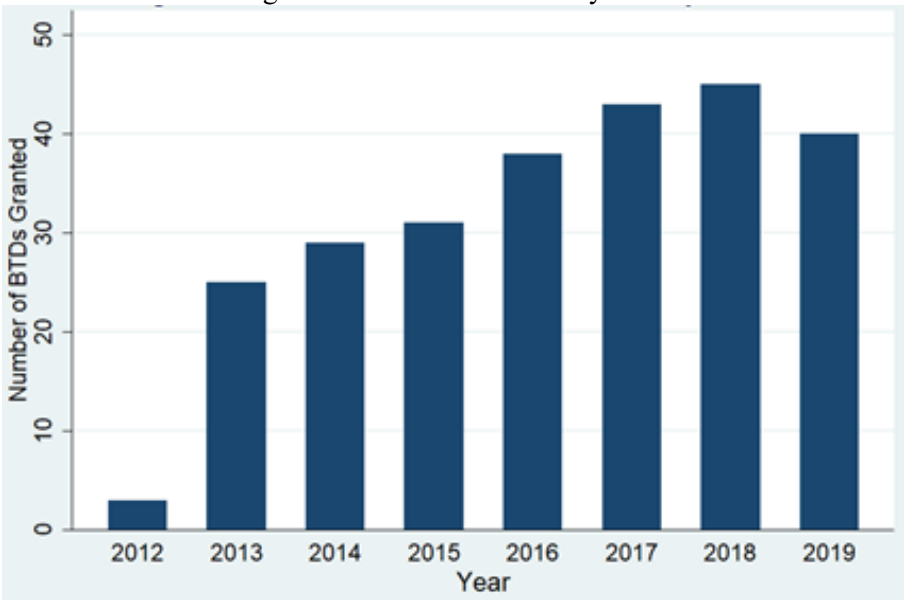
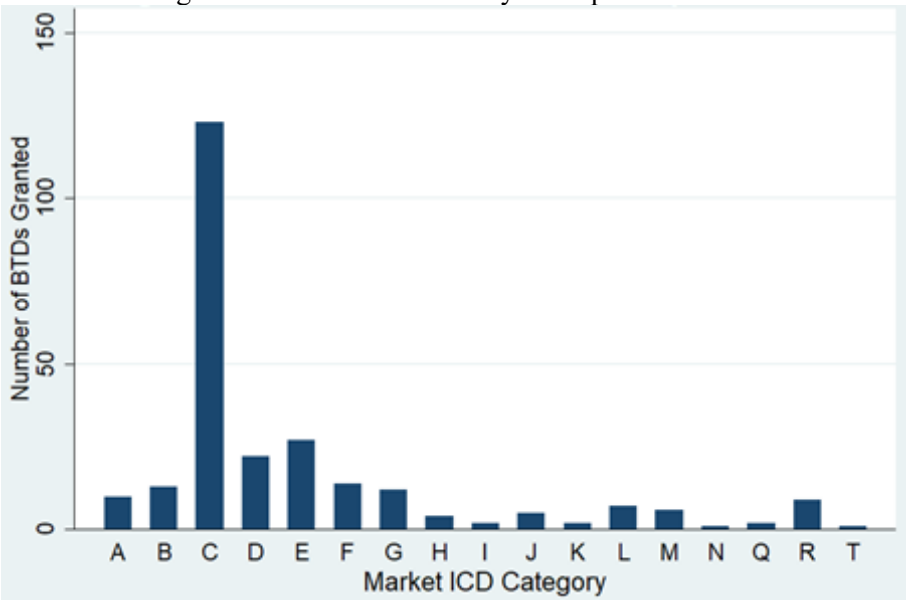


Figure I.C.1.B: Distribution by Therapeutic Market



Section I.C.3: Patient, Physician, and Industry Views of BTDs

Demand for pharmaceutical products is primarily driven by prescriptions from physician office visits.[8] In addition, patients may request of physicians specific drug prescriptions, especially for brand name drugs (Campbell et al. (2013)). This suggests that the demand for pharmaceutical drugs depends to a large extent on the perception of the best available treatment by both physicians and patients.

Abola and Prasad (2016) find that describing drugs using words such as "breakthrough" creates public perception that suggests scientific victory and miracle cures. Krishnamurti et al. (2015) survey a random sample of 597 Americans and find that the term "breakthrough" increased people's belief in a drug's effectiveness and participants were more likely to choose such a drug to treat a deadly condition over a drug without such description. This perception is not limited to the general public as some studies have also found that health professionals and physicians can also perceive breakthrough drugs to be substantially better than existing therapies. For example, Kesselheim et al. (2016) analyze survey data from 692 physicians and find that physicians were more likely to prescribe the breakthrough drug for their patients than the alternative treatment, and conclude that the choice of the term "breakthrough" may lead physicians to overprescribe the drug.

The perceived superiority of BTD drugs is reinforced by their extraordinary effectiveness in some cases. For example, Zoulim et al. (2015) find that Gilead Sciences' Hepatitis C BTD drug, Harvoni, cures over 95% of most patient populations while simultaneously reducing the treatment to 12 weeks compared with the 45% cure rate and the 6-12 months treatment duration for previous therapies. BTD drugs are also likely to boost the revenues of their owners. For example, Merck's Keytruda, approved in 2015, accounted for 23% of Merck's total revenues in 2019. Additionally, a report by Evaluate Vantage Pharma which ranked the drugs approved in 2017 by expected 2022 sales, found that 7 of the top 10 drugs were BTDs.[9]

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[8] For example, the CDC estimates that in 2016, the number of drugs prescribed through physician office visits was about 3 billion units compared to 359 million units prescribed at hospital emergency department visits. Source: https://www.cdc.gov/nchs/fastats/drug-use-therapeutic.htm

[9] These are Ocrevus, Dupixent, Durvalumab, Niraparib, LEE011, KTE-C19, and Ingrezza. Source: Helfand, Carly. "The Top 10 Drug Launches of 2017." *FiercePharma*, 30 Jan. 2017, www.fiercepharma.com/special-report/top-10-drug-launches-2017.

Section I.C.4: FDA Approval Likelihood of BTD Projects

Given BTDs are granted earlier on in the development process, there remains uncertainty whether they will be approved-for-sale by the FDA. Nevertheless, we argue that they are still credible indicators of a threat to rivals. First, in untabulated tests we find that FDA approval-to-sell likelihood is higher for BTDs than for matched projects. The matched sample are drugs in the same ICD-10 (i.e., therapeutic) market, and having the same patent status, same initial development status, and similar drug age. Hazards for BTD drugs indicate they are 3.5 times more likely to be approved relative to non-BTD drugs.[10] Second, the literature provides evidence that BTD drugs are more likely than the average drug to receive FDA approval (see for example Hermosilla (2020)), and that they receive FDA approval in a shorter time (see Hwang et al (2018)).

[10] We also run a separate logit model using this randomly matched sample while accounting for the right censoring issue of our data by dropping drug projects that started development after 2017Q4, and find similar results.

Appendix I.D: Supplementary Results for the BTD Grant Announcement Returns Tests

In this appendix we provide supplementary results for the cumulative abnormal returns analysis. The sections in this appendix are ordered as follows:

- Section I.D.1: Summary and Univariate Statistics on BTD Firm, Rival, and Control Firm Cumulative Abnormal Returns
- Section I.D.2: BTD Announcement Returns Conditional on Market Competitiveness

Section I.D.1: BTD Firms, Rivals, and Control Firms' Cumulative Abnormal Returns Summary Statistics

Table I.D.1: BTD Firms, Rivals, and Control Firms' Cumulative Abnormal Returns Summary Statistics

This table provides descriptive statistics for cumulative abnormal returns (CARS) of BTD firms, rival firms and control firms around BTD grant announcements. We calculate CARs around BTD grant announcements using a market model that estimates parameters over the period of trading days [−271, −21], relative to the BTD grant announcement date. CAR1 (CAR2) are calculated for the three trading (five trading) days [-1, +1] ([-2, +2]) event window surrounding the BTD grant announcement. CARs are winsorized at the 1% and 99% levels. Summary statistics and univariate differences are provided conditional on firm type. BTD firms are firms that have received the BTD for a drug on a given BTD grant date. Rival firms are firms that have any drug project that falls in a therapeutic market that experienced BTD entry on a given BTD grant date. Control firms are firms with products that do not target any BTD-shocked markets on a given BTD grant date. Precommercial is an indicator equal to one if a firm does not own any FDA approved-for-sale products, as of the BTD grant date. Commercial is an indicator equal to one if the firm owned at least one approved-for-sale product, as of the BTD grant date. Columns 1-3 provide the average CAR values by firm type, and test whether these values are insignificantly different from zero. Columns 4-6 present univariate differences between the CARs of the different firm types. asterisks indicate statistical significance as: *** p<0.01, ** p<0.05, * p<0.1

	BTD Firms	Rival Firms	Control Firms	(1) - (2)	(1) - (3)	(2) - (3)
	(1)	(2)	(3)	(4)	(5)	(6)
CAR1	0.017***	-0.004***	-0.004***	0.021***	0.020***	0.000
CAR2	0.022***	-0.003***	-0.005***	0.026***	0.027***	0.002**
Commercial CAR1	0.007**	-0.002***	-0.002***	0.010***	0.010**	0.000
Commercial CAR2	0.008*	-0.002*	-0.004***	0.010**	0.012**	0.002**
Precommercial CAR1	0.043***	-0.007***	-0.004***	0.051***	0.048***	-0.003*
Precommercial CAR2	0.062***	-0.006***	-0.006***	0.070***	0.068***	0.000
Num of Observations	187	5,084	72,097	-	-	-

Section I.D.2: BTD Announcement Returns Conditional on Market Competitiveness

Table I.D.2: Stock Returns of Rivals around BTD Announcements Conditional on Market Competition Levels

The analysis sample has an observation level of firm-market-btd announcement date. The sample includes only rivals and control firms. The sample is primarily focused on smaller rivals that operate in 5 or less markets (5 is the bottom quartile of the number of firm-markets in the sample). Furthermore, a firm-market observation is only included if the firm had at least 10% of their drugs in that market (10% was the top quartile cutoff for market exposure in the sample). The dependent variable is the cumulative abnormal return in the three-day window centered around the BTD announcement. We drop all BTD firm observations in the quarter that they are awarded a BTD. We also drop all rival-market observations for unshocked markets if the same rival was shocked (in a different market) on the same day (e.g., if rival A who operates in markets X and Y was shocked in Y and not in X, I drop the rival A-market X observation on the same day that market Y was shocked). Finally, we drop firm-market observations where another significant corporate event had occurred (e.g., merger, CEO indictment…etc.). We winsorize CARs at the 1% and 99% levels. Next, we sort the resulting sample into medians by the level of market competition. That is, in the columns titled Low Competition, the firm-market-BTD date observations are included if the market falls in the bottom half of competition levels in the sample (vice versa for high competition). The regressions below include the following FE in all regressions: firm times market, calendar quarter, market times calendar quarter. Standard errors are clustered by firm.

	Market Competition	
	Low	High
	(1)	(2)
Rival	-0.024***	-0.003
	(-2.657)	(-0.892)
Observations	74,847	72,805
R-squared	0.054	0.039

Appendix I.E: Supplementary Results for the Phase-II Development Tests

In this appendix we provide supplementary results for the phase II development tests. The sections in this appendix are ordered as follows:

- Section I.E.1 Phase-II development: likelihood of, and cumulative hazards of, development continuation, and the relationship with competition
- Section I.E.2: Time Trends in Phase-II Development Using Projects Initiated Before the First BTD Shock
- Section I.E.3: Constructing the Alternative Sales-Based HHI Competition Measure

Section I.E.1: Phase-II development: likelihood of, and cumulative hazards of, development continuation, and the relationship with competition

Figure I.E.1: Likelihood of Continuing Phase-II Development

These figures plot the percentage of all projects that reported a continuation in the development of phase-II projects.

Figure I.E.1.A: Phase II Development by Mkt Shock

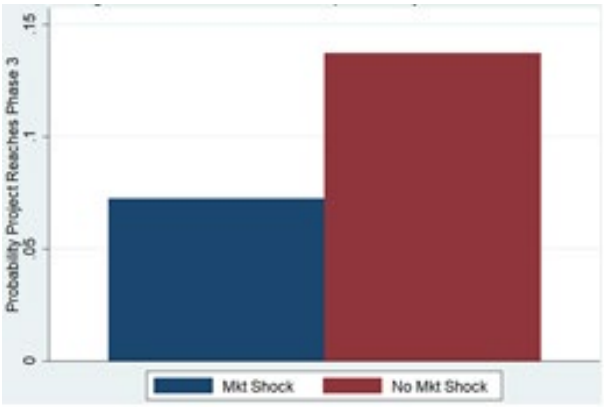


Figure I.E.1.B: Phase II Development for High/Low Competition

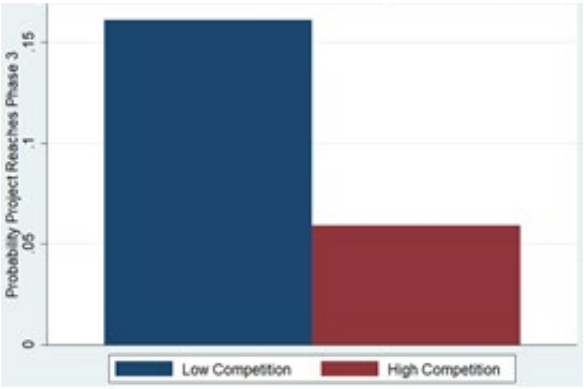


Figure I.E.2: Cumulative Hazard Function of Continuing Phase-II Development

These figures plot the cumulative hazard function (CHF) of the likelihood a phase-II project continues development conditional on the number of quarters the project has been in phase-II.

Figure I.E.2.A: Unconditional Hazards

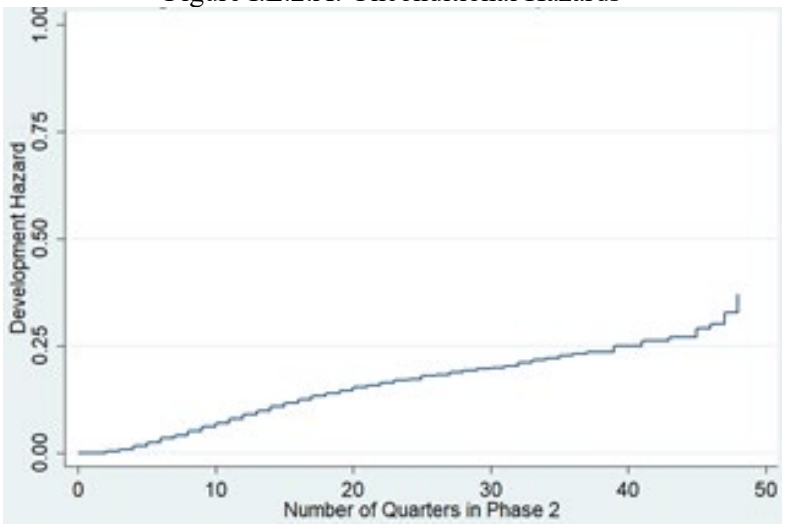


Figure I.E.2.B: by Mkt Shock

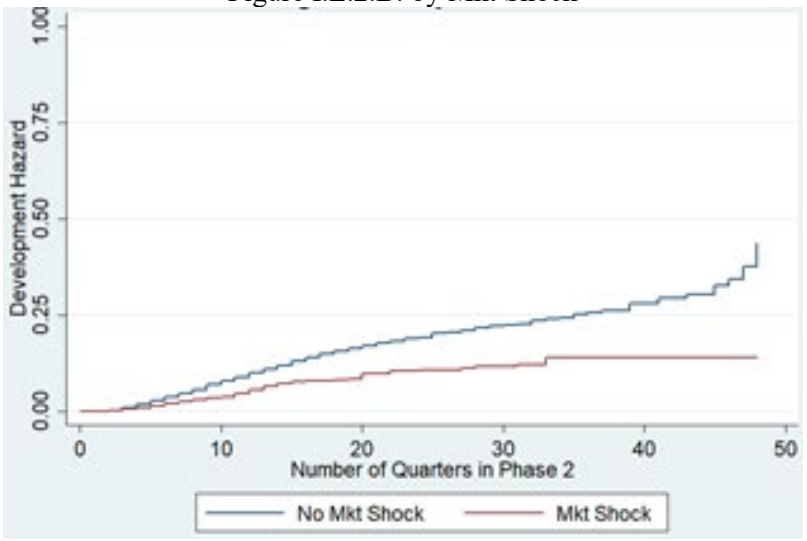
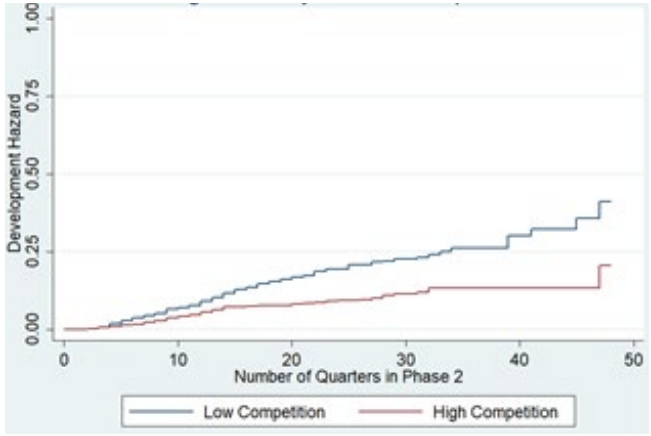
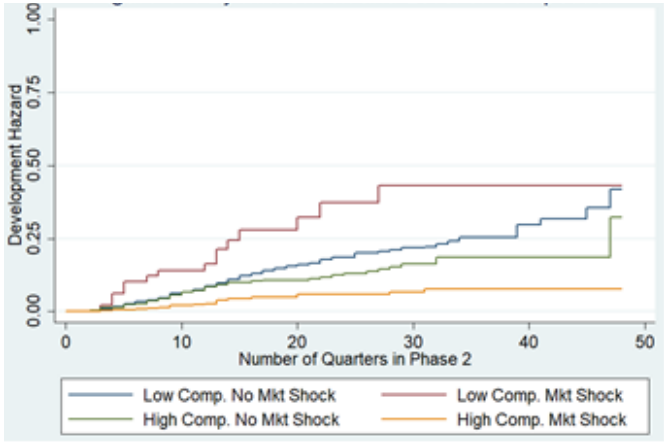


Figure I.E.2.C: by Level of Competition

Figure I.E.2.D: Mkt Shock and Level of Competition


Development Hazard
0.00
0.25
0.50
0.75
1.00
0
10
20
30
40
50
Number of Quarters in Phase 2
Low Competition
High Competition


Development Hazard
0.00
0.25
0.50
0.75
1.00
0
10
20
30
40
50
Number of Quarters in Phase 2
Low Comp. No Mkt Shock
Low Comp. Mkt Shock
High Comp. No Mkt Shock
High Comp. Mkt Shock

Section I.E.2: Time Trends in Phase-II Development Using Projects Initiated Before the First BTD Shock

Figure I.E.3: Trends in the Likelihood of Phase-II development Around BTD Entry

The graphs in this figure display the change in the likelihood of phase-II graduation around BTD events. The graphs are based on the same analysis used in Figure 2 of the main paper, but with one difference: ever-shocked phase-II projects are only included if they were initiated before the first BTD shock was awarded to any product in the targeted market. That is, the analysis sample includes all the never-shocked projects from the sample of Figure 2, and only the ever-shocked projects that started phase-II trials before the first shock. The legend of Figure 2 of the main paper includes more details on the sample and the methodology.

Figure I.E.3.A: Full Sample

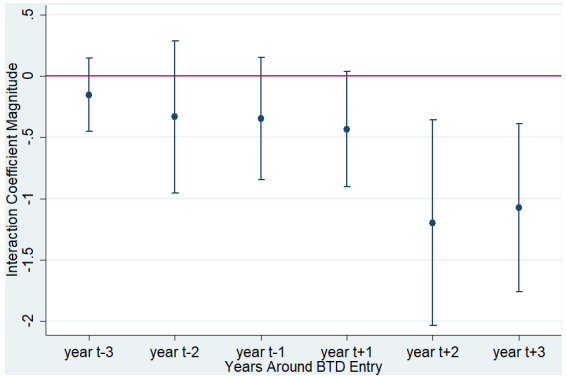


Figure I.E.3.B: Low Median of Competition Subsample

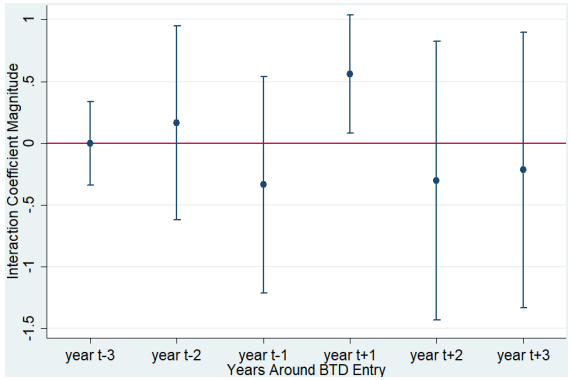
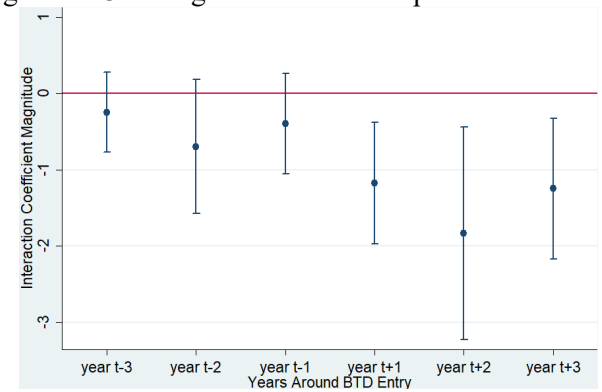


Figure I.E.3.C: High Median of Competition Subsample



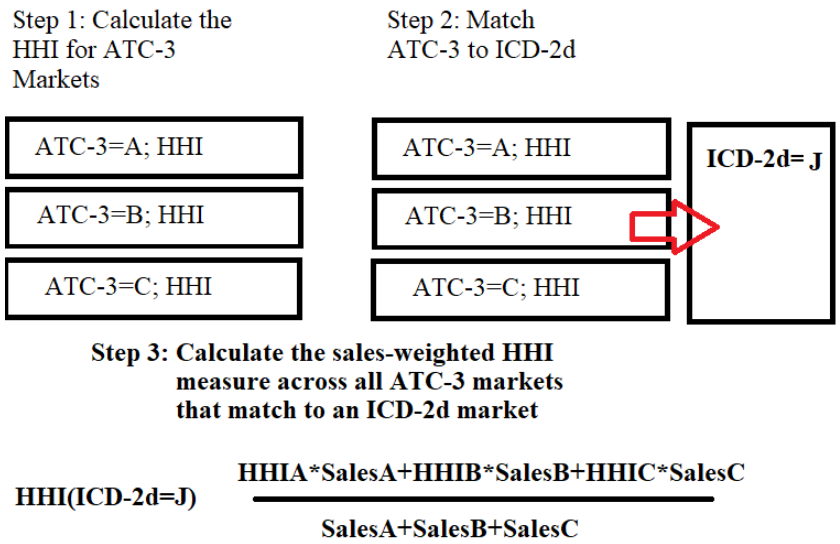
Section I.E.3: Constructing the Alternative Sales-Based HHI Competition (i.e. Concentration) Measure

In this section we first provide details on the construction of an alternative (inverse) competition measure; a sales based HHI concentration measure. Then we show that this sales-based concentration measure is significantly and negatively correlated with our original competition measure.

Our original competition measure, defined as the natural log of the number of drug projects within a therapeutic market, does not include information on the level of sales within an industry. We construct the alternative sales-based concentration [i.e. inverse-competition] measure, and replicate our baseline results of tables 5 and 6 in the main paper. Details on the construction of this alternative measure as well as cross-validation tests with the original competition measure are provided in this section. The revisiting of main results using the alternative concentration measure are provided in section D6. We create the concentration (i.e. HHI) measure as follows:

1. We start with the Medicaid State Drug Utilization Data (herein SDUD), which reports the total sales and total units dispensed for a drug on a quarterly basis. In the SDUD drugs are identified using the National Drug Code (NDC) code which is issued by the FDA to uniquely identify drugs. The NDC code is a 3-segment code: the 1st segment is for the labeler (manufacturer) of the drug, the 2nd segment is for the product, and the 3rd segment is for the package.
2. We identify the correct drug manufacturers by using the data from Hammoudeh and Nain (2021) who use the SDUD data to examine drug prices around mergers and acquisitions. This results in identifying about 700 unique drug manufacturers who sold products to Medicaid from 2010q1 to 2020q2.
3. We match the NDC code to the WHO's Anatomical Therapeutic Chemical Classification System (ATC) codes using the NDC-to-ATC cross-walk provided by Kury and Bodenreider (2017). ATC codes are a drug classification system that are controlled by the World Health Organization and that classify the active substances of a drug based on the organ or system on which the drug acts and the drug's pharmacological and chemical properties. The active substances are classified in a hierarchy with five different levels. The first level defines the 14 anatomical groups, e.g. cardiovascular system is assigned code C. The second level defines the pharmacological or therapeutic subgroup, e.g. calcium channel blockers are assigned code C08. The third defines the pharmacological subgroup, e.g. selective calcium channel blockers with direct cardiac effects are assigned code C08D. The fourth level defines the chemical subgroup, e.g. Phenylalkylamine derivatives is assigned code C08DA. Finally, the fifth level provides information on the chemical substance, e.g. Verapamil is assigned code C08DA01.

4. We create the HHI index using the third level ATC codes (ATC-3). The HHI is calculated as the sum of squared market shares for each firm-quarter in an ATC-3 category. We choose ATC-3 because it achieves the right balance between providing enough information about a market and allowing for a sufficient number of matches with the Cortellis data (explained in step 5 below).
5. We use the cross-walk between ATC-3 codes and ICD-10 codes. This cross-walk was created by first scraping http://hulab.rxnfinder.org/, then scraping https://icdcode.info/ when the first site did not produce a match. The ATC-to-ICD10 cross-walk is a one-to-many cross walk (i.e. one ATC-3 code can match up to 31 ICD-10 codes). This is because the ATC codes rely more on the chemical structure to classify a drug, whereas the ICD-10 codes classify drugs based on a medical condition, and one chemical structure can be used to address several medical conditions.
6. ICD-10 are five-digit codes in the form of XNN.NN, where "X" is a letter, and "N" is a number. The first digit "X" is the general category. There are 26 general categories, e.g. cancer is C. The second digit defines the organ system of the drug, e.g. both melanoma and skin cancer (both are forms of skin cancer) have a 2-digit ICD-10 code of C4. The third digit provides more details on the organ, e.g. Spleen cancer has a 3-digit ICD-10 code of C26, whereas pancreas cancer's code is C25. Finally, the last two digit of the ICD-10 code provide very specific information on the disease, e.g. Non-small cell lung cancer has a full ICD-10 code of C34-90, whereas small cell lung cancer's code is C34-91.
7. Given the information in (6) above, and the limitations of the ATC-ICD-10 cross-walk, we consider matching ATC-3 codes to either two-digit (ICD-2d) or three-digit (ICD-3d) ICD-10 codes. When matching ATC-3 codes to ICD-2d, 79% of the ICD codes are matched, whereas when matching ATC-3 codes to ICD-3d only 42% are matched.
8. Given the low percentage match when using the ICD-3d codes, we focus on ICD-2d for calculating the ICD-based HHI measure. ICD-2d codes capture the general area. ICD-2d codes (for example) will not tell us the concentration of the melanoma market, but it will tell us the concentration of the more general skin cancer market.
9. Since an ICD-2d market can match to multiple (up to 31) ATC-3 codes, we find the HHI of an ICD-2d market by calculating the sales-weighted averages of the ATC-based HHI across all ATC-3 markets that match to a ICD-2d. The figure below illustrates how this is done in 3 steps. More competitive markets under our original measure, associate with less concentrated markets under the sales-based HHI measure. This supports our use of drug project count in a therapeutic area as a good proxy for that product market's competitiveness, especially given the limitations of drug sales information / data.



Step 3: Calculate the sales-weighted HHI measure across all ATC-3 markets that match to an ICD-2d market

$$\text{HHI(ICD-2d=J)} = \frac{\text{HHIA*SalesA+HHIB*SalesB+HHIC*SalesC}}{\text{SalesA+SalesB+SalesC}}$$

Table I.E.1 provides summary statistics on the ICD-2d HHI competition measure and cross validates this with the original competition measure. The results in panel B of Table B3 in the main paper's Appendix B indicate that the HHI concentration measure is significantly negatively correlated with our main/original competition measure.

Table I.E.1: Sales-Based HHI Measure Comparison to the Original Competition Measure

This table presents summary statistics on the ICD-2d HHI competition measure (Panel A) and cross validates this measure with the original competition measure (Panel B). The sample includes observations at the ICD-2d-quarter level. Panel B presents the results from an OLS regression of the HHI competition measure on the original competition measure. The regression includes ICD-2d fixed effects, quarterly fixed effects and robust standard errors. T-stats are presented in parentheses and asterisks indicate statistical significance as follows: *** p<0.01, ** p<0.05, * p<0.1

Panel A: Summary Statistics of HHI

	(1)
Mean	0.257
25th Percentile	0.182
Median	0.237
75th Percentile	0.311
Standard Deviation	0.114
Correlation with Original Competition Measure	-0.06

Panel B: Regressing HHI on Original Competition Measure

	(1)
Original Competition Variable	-0.023***
	(-3.541)
Constant	0.492***
	(21.268)
Observations	6,081
R-Squared	0.789