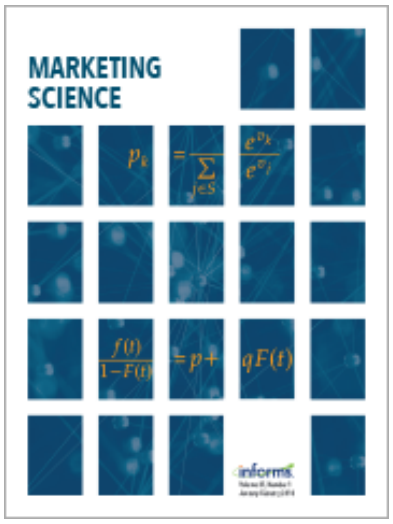

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Strategic Research and Development Investment Decisions in the Pharmaceutical Industry

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Abstract. Do pharmaceutical firms respond to the actions of their competitors in research and development, and if so, how much? Answering this question has implications for policies aimed at incentivizing drug development, such as greater exclusivity protections and a faster Food and Drug Administration approval process. Although such policies lead to quicker realization of profits and/or more time to earn profits, they also intensify competition, thereby reducing per-firm profits. Which effect dominates depends on the degree of competition. To this end, I estimate a dynamic investment model using Phase 3 data. Solving the new equilibrium, I find that even though an expedited process and longer periods of market exclusivity increase competitive intensity, it could prompt increased entry into Phase 3, thereby encouraging innovation.

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Supplemental Material: Data and the online appendix are available at https://doi.org/10.1287/mksc.2020.1224.

Keywords: competitive analysis • dynamic programming • empirical IO methods • innovations • public policy • legal

1. Introduction

Pharmaceutical firms spend a significant portion of their time and investment in the research phase testing and proving the safety and efficacy of their drugs. The profits are realized only upon launch of the product, so drugs that fail partway through the process generate no revenues to offset the substantial costs accumulated over the development process. Finally, unlike most industries, even after significant investment and results, the launch of a firm's product in a market is not certain. This is because the Food and Drug Administration (FDA), the regulatory authority that oversees research and development (R&D) testing in its entirety, can approve or reject a firm's petition to launch in the market. The outcome of this regulatory process is fairly uncertain, with unpredictable review times.[1] Pharmaceutical firms view this process as delaying marketing of their new drugs and deterring innovation.[2] This effect is further exacerbated by the short remaining patent life of most drugs.[3]

The market exclusivity granted by the FDA upon a drug's approval is designed to offset the time spent by firms in lengthy clinical trials and awaiting regulatory approval. This period of exclusivity is granted irrespective of the number of patent years remaining. However, many firms have argued the current market exclusivity period of 5 years (for new chemical entities) is insufficient. For example, one of the proposals in the 21st Century Cures Act was to increase the market exclusivity period to 15 years (Gaffney 2015). This proposal did not make it to the final act.

In addition, many firms, investors, and industry lobbyists have repeatedly called for a faster FDA approval process. The recently enacted 21st Century Cures Act is geared toward such an acceleration, with its goal being to ensure patients get earlier access to treatments (Califf 2016). However, opponents have called the act a "gift" to the pharma lobby at the cost of safety.[4]

Whether pharma companies actually benefit from these policies—longer market exclusivity and expedited approval—is unclear. From the perspective of a focal firm, longer market exclusivity is beneficial because the firm has more time to earn profits before generic entry, and an early launch is beneficial because these profits are realized sooner. However, the possibility of longer market exclusivity and an early launch make the market lucrative to other firms as well, potentially leading to a more crowded market, reducing the focal firm's profits.[5] Thus, although these policies can increase the net present value of profits, it can also intensify competition among firms, leading to lower per-firm profits. Which effect dominates depends on the extent to which firms are impacted by competition. Ching (2010a) analyzed such a trade-off in the context of generic drug entry, where expediting FDA approval for generic drugs increases not only

the likelihood that they enter earlier but also the likelihood that they enter crowded markets, thereby decreasing their profitability. This paper looks at a similar effect but on R&D decisions, which have implications for innovation and new product entry. The theoretical literature does not provide a clear direction of the impact of competition on innovation: on the one hand, competition can encourage innovation if the potential innovator is able to usurp market share from the incumbent with its new product, but on the other hand, the presence of competition can deter the incentive to innovate if the potential innovator is able to take only a share of the total industry profits.[6]

Using data to empirically measure this impact is hard because observed market structure and innovation rates are equilibrium responses and hence codetermined. The ideal way to measure the impact of competition on innovation is by observing market structure change for exogenous reasons. Empirical work that uses this strategy includes Aghion et al. (2004), who use changes in market structure caused by government policy changes, and MacDonald (1994), who uses changes in import policies. However, exogenous variation of market structure in most industries is scant. Without such variation, regressing the existing market structure on investment would be uninformative because observed investments are equilibrium responses. Cockburn and Henderson (1995) point this out as a hypothesis they cannot reject even when they find only a weak correlation in investment across firms (i.e., firms are not influenced by competitors behavior). This calls for a structural model that endogenizes market structure and innovation, taking into account industry-specific features (e.g., Goettler and Gordon 2011). I use both approaches to measure this impact, relying on the structural parameters to evaluate the counterfactual of a longer market exclusivity and a faster FDA approval process.

First, in a reduced-form regression, I measure if firms respond to competitors' states. To get around the endogeneity of market structure and investment, I exploit a unique feature of the pharmaceutical industry—the uncertainty of the FDA approval process. Although firms might know the average approval probabilities in expectation, the exact outcome of the FDA review process is uncertain (i.e., FDA approvals and rejections conditional on filing are fairly exogenous). A similar argument has been made in Ching (2010b) and Reiffen and Ward (2005), who use the random nature of generic approvals to identify the effect of competition on price. In this regression, I find evidence that firms respond to competitors' states, and competition has a negative impact on investment: specifically, a firm's probability of continuing investment decreases if the firm's competitor received an FDA approval and increases if the competitor received an FDA rejection.

Second, I build a structural model that accounts for the endogeneity of market structure and innovation. Using a data set on firm entry, continuation, and exit decisions in Phase 3 clinical trials across different markets in the pharmaceutical industry, I estimate a structural model to measure the impact of competition on firms' continuation decisions. The structural model takes four main aspects of the pharmaceutical industry into account: the forward-looking behavior of firms, their strategic decision making, market heterogeneity, and the uncertainty of the FDA approval process. Because firms incur huge costs in the research phase, which can take up to 10–12 years, and because profits are realized only upon successful launch of the product, it is the forward-looking nature of firms that justifies investing large amounts in the research phase. Thus accounting for dynamics in modeling this industry is important. Second, the model should be able to account for equilibrium responses of firms. For example, a firm may exit a market while in the research phase if it observes that one of its competitors has launched. This is because if the share of profit of the focal firm decreases with the number of launched firms, it no longer justifies continued investments in the research phase. Third, one needs to account for the fact that some markets can be more lucrative than others by accommodating the presence of unobserved heterogeneity in markets. Finally, the launch outcome is not determined by the firm but by the FDA review process. To account for all the above-mentioned features of the pharmaceutical industry, I estimate a dynamic oligopoly model allowing for unobserved heterogeneity.

I estimate the model using the underlying approach outlined in Arcidiacono and Miller (2011). The estimation recovers two types of markets, and the estimates indicate a significant and negative impact of competition on firms' investment decisions. I use these estimates to solve for the dynamic equilibrium under longer exclusivity periods and a faster approval process. I simulate the effect of a faster FDA approval process by reducing the probability that a drug remains in review but keeping overall approval and rejection rates the same.

The results indicate an expedited approval process encourages entry: although per-firm profits decrease, the quicker access to profits outweighs the loss from the increased competitive intensity. Increasing market exclusivity also encourages innovation but at a lower rate than under a faster approval process. Although increased exclusivity gives more time for the firm to earn profits, these profits are further into the future. On the other hand, a faster approval process gives firms quicker access to the market. In both cases,

I find that ignoring these strategic considerations in R&D leads to overestimating the benefit of these policies: the expected value of entering Phase 3 is overestimated by 1.3%–6.8% when strategic responses are not accounted for.

1.1. Contribution

This paper is broadly related to the literature on firm strategic behavior. Within the pharmaceutical sector, this literature has focused largely on the impact of competition from generic entry on branded drugs' pricing and advertising levels (e.g., Caves et al. (1991), Ching (2010a), and Ellison and Ellison (2011)) and more recently on firms' strategic detailing behavior (e.g., Liu et al. (2016)). Closely related is the paper by Ching (2010a), who develops a dynamic oligopoly structural model to study the entry decisions of generic firms. Similar to the setting in this paper, these firms face randomness in the approval timing of the FDA. However, little research exists on firm strategic behavior *prior* to the launch stage, when firms' products are not yet in the market. This paper finds evidence suggesting strategic behavior in the prelaunch stage, and it investigates the implications of such strategic effects on the implementation of an expedited approval policy.

Outside the pharmaceutical sector, papers that have empirically studied R&D investment decisions in a competitive environment have done so from the perspective of postlaunch activities such as advertising, learning about demand uncertainty, and brand building (e.g., Dubé et al. (2005), Hitsch (2006), Ellickson et al. (2012), Vitorino (2014), and Borkovsky et al. (2017)). R&D investments that influence new product launches[7] have received relatively little empirical attention, primarily because of a lack of data that allow one to observe R&D efforts prelaunch. For this reason, the intersection of innovation, new product development, and competitive behavior has largely been studied from a theoretical perspective (e.g., Goettler and Gordon (2014) study the impact of entry costs and competition on investments in the context of a nondurable good; Hauser et al. (2006) provide a comprehensive review of other theoretical work in the marketing literature.)

Another related paper is Goettler and Gordon (2011), who estimate a structural model that endogenizes innovation to evaluate the counterfactual of whether Intel would innovate more in the absence of AMD. Unlike their setting, where the market structure is fixed at two firms, I observe varying market structures both within and across markets. This approach allows me to infer the degree of competition from firms' exit decisions rather than relying on product substitution in the postlaunch market. This feature is especially important in the pharmaceutical industry, where a large number of molecules (nearly 95% in the data) do not reach the launch stage.

The rest of this paper is organized as follows. Section 2 gives an overview of the pharmaceutical industry, describes the data, and highlights a few empirical regularities in a reduced-form setting, Section 3 builds the structural model, Section 4 discusses the estimation strategy, and Section 5 presents the results. Section 6 evaluates the counterfactual of a faster approval process and that of longer market exclusivity, and Section 7 concludes.

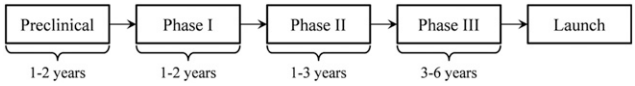
2. Industry Background and Data

Drug development is a time-intensive and expensive process. Firms vying to enter a market after discovery of a chemical compound have to perform preclinical, Phase 1, Phase 2, and Phase 3 trials before they can launch their product. Getting to the final launch phase is a low-probability event—for every 250 compounds that enter preclinical testing, only one gains FDA approval.[8]

Preclinical trials for the drug involve testing the compound on animals. On the basis of the findings, firms may decide to file an investigational new drug filing with the FDA, which can either approve or reject the filing. If approved, the drug has to pass successfully through three more phases: Phase 1, which involves testing on a small group of healthy individuals; Phase 2, which involves testing on a small group of patients with the disease to prove the drug has the intended effects on the patients; and Phase 3, which involves large-scale testing to establish the safety and efficacy of the drug. Figure 1 illustrates the various phases a pharmaceutical firm needs to go through before final launch and the approximate time it takes to complete each phase.

To answer the questions posed in this paper, we need firm actions in the R&D stages prior to a new drug application (NDA), as well as FDA-determined launch outcomes at the market-firm-year level. I focus on drug-development efforts post-Phase 2 clinical trials.[9] This is because Phase 3 is by far the most expensive of all four research phases (DiMasi et al. 2003) and because these data are largely publicly available because the FDA requires that all drugs in a controlled clinical investigation other than Phase 1 trials be registered on a publicly available database. The data set used in the paper comes from Adis R&D

Figure 1. Pharmaceutical Research and Development Process



Insight, an aggregator that collects this information across all firms and markets over time.

Specifically, an observation in the data consists of the date a firm entered Phase 3 clinical trials in a particular disease indication and the date if it exited, filed, or launched. The data consist of a total of 294 disease indications[10] in the period 1995–2008. Markets were classified by how firms defined their research. In most cases, this procedure led to a one-to-one mapping between disease indication classifications and markets. In a few instances, manual coding was required to classify similar disease indications into a single market. For example, the coded market for type 1 diabetes is sometimes referred to as type 1 diabetes and other times as type 1 diabetes mellitus in the raw data. I supplement these R&D data with data from CenterWatch,[11] which has a list of medical conditions and their corresponding therapeutic area classifications, resulting in a total of 27 therapeutic areas.

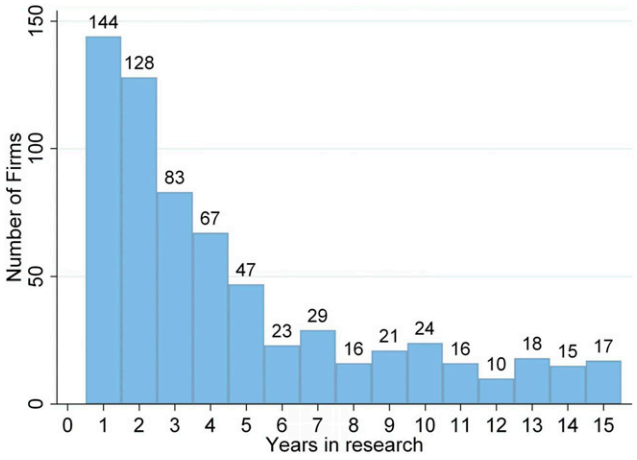
The R&D investment data are further supplemented, where available, with market-specific descriptives such as prevalence and whether the indication disproportionately affects people of a specific age, race, or gender. These data come from epidemiology reports from MedTrack, publicly available government data sources such as the National Institutes of Health (NIH) and the National Cancer Institute's Surveillance, Epidemiology, and End Results database, as well as medical journal articles. Finally, data from MedTrack, which tracks realized sales of launched products, provide a crude measure of the indication-specific market size in dollar amounts. These figures are observed only conditional on launch; however, averaging across all drugs and years of realized sales within a disease indication gives an approximate measure of the market potential specific to a given indication.

The pharmaceutical industry is characterized by four main features: forward-looking firms, heterogeneous markets, uncertainty in FDA outcomes, and strategic firms. I now provide evidence of each of these characteristics from the data.

2.1. Forward-Looking Firms

Firms spend an average of 4.6 years in Phase 3 clinical trials. Figure 2 shows the number of years various firms across different markets spend in research. During this period, the firm does not earn any profits. Investments are made in expectation of profits if and when a firm's drug launches in the market. This is clear evidence of firms' forward-looking behavior and warrants a model that takes these dynamics into account.

Figure 2. (Color online) Distribution of Years Spent in Research Across All Firms and Markets



2.2. Heterogeneous Markets

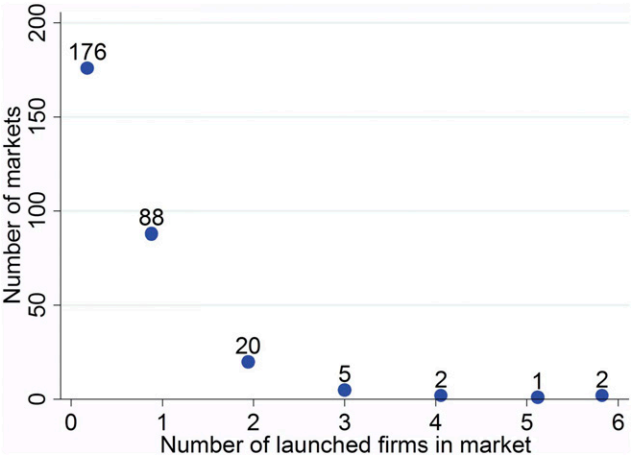
The number of drugs in Phase 3 trials per market ranges from 1 to 10: Table 1 shows the distribution of the number of drugs per market; 52% of markets have just one drug that has entered Phase 3 in that indication, whereas few markets have more than four drugs that entered the market. This is an indication of substantial market-specific heterogeneity: some markets see more firms investing in them, whereas others see relatively fewer firms.

This market-specific heterogeneity is also evidenced in the number of launched firms per market, shown in Figure 3. The average number of launched firms in a market is 0.57, with 176 markets having no launched product during the time span in the data, 88 markets having one firm that has launched successfully, 20 markets with two launched firms, and 10 markets with greater than three launched firms. Characteristics such as prevalence; whether the disease is more likely to affect people of a specific age, race, or gender; and a rough measure of market size as imputed by sales conditional on launch also vary by market, as shown in Table 2.

Table 1. Number of Drugs in Research per Market

Number of drugs per market	Number of markets	% of markets
1	152	52
2	56	19
3	35	12
4	21	7
5	8	3
6	7	2
7	4	1
8	6	2
9	2	1
10	3	1

Figure 3. (Color online) Number of Launched Firms per Market



2.3. Uncertain FDA Approval Process

After entering Phase 3 clinical trials, a firm in a market can take one of three actions: continue investment (i.e., remain in Phase 3), exit the market, or file for an NDA. After a firm files with the FDA, whether the firm's petition is approved, is rejected, or remains in further review is entirely determined by the FDA. Table 3 summarizes the transitions between phases across all drugs, markets, and time. The second row of the table is indicative of firms' endogenous actions: 86.9% of the time, an incumbent continues in its R&D efforts; 7.6% of the time, it files for an NDA; and 5% of the time, it decides to exit the market. The third row is indicative of the FDA-determined exogenous outcomes: of those that are filed, 26.2% are approved, 2.3% are rejected by the FDA, and 71.6% continue to remain in review. Both this and Figure 4, which shows the distribution of years spent in review across all firms in the data, indicate (1) approval on filing is not guaranteed and (2) realization of the outcome is not always quick. Conditional on an outcome (i.e., approval/rejection), the median (average) time spent in review is 14 (18.7) months. The FDA's database (FDA 2016) provides statistics on the median review time, defined as the length of time it takes to review a new drug application and issue an action letter. Per this database, the median time spent in review was 20.8 months in 1993 and 12.5 months in 2009, the last year of the data set used in the paper. These numbers mirror the statistics of the data set closely.

2.4. Strategic Interactions Between Firms—Reduced-Form Evidence

I now provide reduced-form evidence showing the impact of competitors' states on a firm's investment decisions. Table 4 regresses the decision to continue or exit on the firm's own state as well as the competitor's state, controlling for market, firm, and time fixed effects. The first set of results under the column "Endogenous actions" shows that a firm is more likely to continue investment if a competitor has exited the market, and this probability increases as the number of competitors that have exited the market increases. The second column includes the FDA-determined outcomes of approvals and rejections. The results indicate that a firm is less likely to continue investment in R&D when a competitor has launched successfully in the market, with more competitors having an increasingly negative effect. The results also indicate endogenous as well as FDA-determined exits have a similar effect on a firm's decision to continue investment.

Endogeneity concerns stem from two sources: (1) firm-determined outcomes are equilibrium responses, and (2) an omitted variable, such as a scientific discovery specific to a disease market, can lead to biased estimates. Concerns related to (1) are mitigated by the regression on FDA-determined outcomes. To the extent that the firm files only if it expects a positive outcome, this can still be at best interpreted as a correlational regression. To overcome this concern, I turn to a structural model in Section 3 that explicitly endogenizes firm actions. Concerns related to (2) should lead us to underestimate the effect of competition leading to an upward bias of the estimate. To see this, a market-time-specific event, such as a scientific discovery that makes Phase 3 clinical trials easier for all firms, will likely cause us to see more launched firms in the market and more firms investing in R&D efforts. This will lead to a positive

Table 2. Market Characteristics

	Mean	Std. dev.	Percentiles 10th	Percentiles 50th	Percentiles 90th	No. of observations
Prevalence (per 10,000)	628	1,056	0.74	130	2,000	158
Varies with						
Age	0.25	0.43	0	0	1	215
Race	0.41	0.49	0	0	1	215
Gender	0.53	0.50	0	0	1	215
Market size ($ millions)	468	438	41	349	1,054	213

Table 3. Phase Transitions Across All Drugs, Firms, Market, and Years

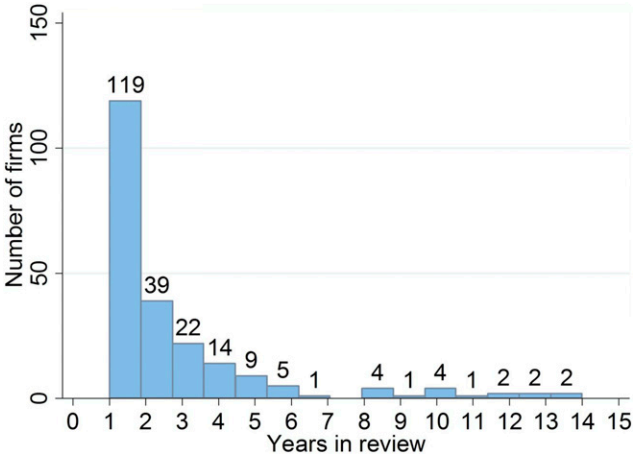
	Not entered (%)	*Entered Phase 3* (%)	*Filed NDA* (%)	*Launched* (%)	*Exited* (%)	No. of observations
Not Entered	84.7	15.3	0	0	0	3,912
Entered Phase 3	0	86.9	7.6	0.6	5.0	3,045
Filed NDA	0	0	71.6	26.2	2.3	573
Launched	0	0	0	100	0	1,213
Exited	0	0	0	0	100	1,188

coefficient on the *Number of competitors launched* coefficient, whereas the estimated coefficient reported in Table 4 is significantly negative.

Table 5 shows a similar regression but on the decision of when to enter Phase 3 trials. Here, we see a negative impact of the number of firms in research on the focal firm's decision to enter Phase 3, with the probability further declining as the number of competitors in research increases. Surprisingly, we also see that as the number of exits increases, firms are less likely to enter the market. This could be driven by market-time-specific trends or by a learning phenomenon whereby firms learn, from the actions of their competitors, that certain markets are hard to do research in. This could also be because the reduced-form regressions do not account for the fact that the decision to continue and enter are inherently connected. The model in Section 3 allows for this. Including the FDA-determined outcomes, we see that launched competitors have an increasingly negative effect on a firm's decision to enter.

Online Appendix A shows these patterns hold even when all firms (and not just the top 15) are included. Market-specific variables (market potential, prevalence, age, race, and gender) were found to be poor indicators of firms' entry and investment decisions in Phase 3. Online Appendix B shows regressions of firms' endogenous decisions on market characteristics. The coefficients on the market characteristics are insignificant. This is possible because these variables likely affect firms' decisions early on in the drug discovery phase, rather than in late-stage clinical trials. I also find that therapeutic area fixed effects have poor explanatory power. Market fixed effects, on the other hand, have a much higher explanatory power, highlighting the importance of unobserved heterogeneity. Moreover, not including market fixed effects leads to insignificant estimates on competitors' states. This finding informs the structural model, where I recover the estimates by (unobserved) market type instead of relying on market-specific observables in the state space.

Figure 4. (Color online) Distribution of Years in FDA Review Across All Firms and Markets



2.5. Strategic Interactions Between Firms—Anecdotal Evidence

Recap, a company that provides insights for the biopharmaceutical industry, collects reasons as to why firms abandon their compounds in late-stage clinical trials. Their analysis suggests that of the 66 compounds (out of 559 compounds in Recap's Bioportfolio Index, which contains only biotech companies) that abandoned clinical trials in Phase 3, 12% state "pipeline prioritization" as their reason for leaving Phase 3. This includes market and competitive dynamics such as market size and level of market saturation.

Although this provides preliminary evidence of the impact of competition on firms' decisions, the model I develop in Section 3 explicitly endogenizes innovation and market structure, taking into account the specifics of the industry as already described in this section.

2.6. Other Industry Specifics

Additional industry specifics include the following:

Symmetric firms: I focus on the set of drugs affiliated with the top 15 firms, restricting attention to those firms that have similar R&D resources, abilities, and capital. I therefore assume that, conditional on being in a research state, all firms are equal.[12]

Table 4. Decision to Continue or Exit as a Function of Competitors' States

Dependent variable	Endogenous actions		FDA outcomes	
Continue/Exit	Coefficient	*t*-statistic	Coefficient	*t*-statistic
Number of competitors exited				
1	3.00	6.6	3.12	6.54
2	4.66	6.41	4.74	6.48
3	4.96	4.83	5.63	4.93
4	4.67	2.78	4.30	2.6
5	6.37	4.75	5.13	3.39
6	7.63	4.62	4.83	2.63
7	20.23	0.02	18.05	0.01
Number of competitors in research				
1	0.10	0.27	0.02	0.04
2	0.48	0.9	0.23	0.41
3	0.36	0.53	−0.28	−0.38
4	0.98	1.09	0.76	0.74
5	−0.64	−0.5	−1.62	−1.19
6	−1.58	−1.11	−3.04	−1.87
7	0.00		0.00	
Number of competitors in filed status				
1	−0.48	−1.12	−0.52	−1.03
2	−1.33	−1.29	−0.54	−0.49
3	12.33	0	12.99	0.01
Number of competitors exited due to FDA				
1			3.73	2.87
Number of competitors launched				
1			−0.29	−0.49
2			−1.41	−1.59
3			−2.15	−1.99
4			−4.80	−2.73
5			9.33	0
6			−7.89	−3.36
Own state (Reference: *Research year* > 4)				
Research year 1	1.41	3.16	1.33	2.9
Research year 2	0.81	1.98	0.71	1.69
Research year 3	0.64	1.57	0.45	1.07
Research year 4	0.78	1.74	0.71	1.56
Fixed effects	Market, firm, time			
Log likelihood	−218.46		−205.73	
No. of observations	1,159		1,159	
No. of markets	294		294	

Notes. The first column, "Endogenous actions," reports estimates that include only firm-driven outcomes. The second column, "FDA outcomes," includes FDA-determined approvals and rejections (i.e., *Number of competitors exited due to FDA* and *Number of competitors launched*).

Number of firms per market: In the data, 90% of markets (Table 1) have four firms or fewer that have entered the market. I therefore restrict attention to the first four drugs that have entered the market. I also use this data feature in the counterfactual, where I assume there are a total of four firms.

Time to patent expiry: A potentially relevant state variable, *Time to patent expiry*, is unobserved. Collecting such data are not trivial: patents are not tied to a particular molecule/mechanism and are extremely hard to identify from the U.S. Patent and Trademark Office (USPTO) database.[13] However, even though the time to patent expiry is unobserved, the number of years a firm has spent in research is likely to be a good proxy for the time to patent expiry: as the firm spends more years in research, it has less time remaining on its patent.

In addition, for the subset of approved drugs, such data are available from the FDA's Orange Book. I use this subset to estimate whether time to patent expiration has a significant impact on a firm's decision to invest. Online Appendix C describes the data collection and matching process, the estimation procedure and results. I find that (1) the focal firm is no more likely to enter when it has more (versus less) years remaining on its patent, and (2) the leader's (determined ex post using the approved drug) patent expiration has no significant impact on a firm's decision to continue or when it enters.

Table 5. Decision of When to Enter Phase 3 as a Function of Competitors' States

Dependent variable	Endogenous actions		FDA outcomes	
Enter/Not Enter	Coefficient	*t*-statistic	Coefficient	*t*-statistic
Number of competitors exited				
1	−1.33	−4.65	−1.35	−4.59
2	−1.64	−3.68	−1.84	−4.00
3	−2.75	−2.95	−2.96	−3.48
4	0.00	0.00	0.00	0.00
5	−3.14	−2.23	−3.32	−2.25
6	−4.14	−2.40	−3.88	−2.11
7	0.00	0.00	0.00	0.00
Number of competitors in research				
1	−0.61	−3.21	−1.18	−5.86
2	−1.51	−5.62	−2.30	−8.05
3	−1.75	−4.69	−2.52	−6.45
4	−1.60	−3.31	−2.73	−5.60
5	−2.64	−3.17	−3.32	−4.33
6	−2.12	−0.47	−2.75	−1.05
7	−1.21	−1.06	−2.76	−2.38
Number of competitors in filed status				
1	−0.45	−1.97	−1.03	−4.22
2	0.23	0.45	−0.42	−0.88
3	−13.17	−0.02	−12.24	−0.04
Number of competitors exited due to FDA				
1			−3.31	−5.72
Number of competitors launched				
1			−2.27	−7.48
2			−2.97	−6.64
3			−2.57	−3.88
4			−4.06	−3.96
5			−4.53	−3.23
6			0.00	0.00
Fixed effects	Market, firm, time			
Log likelihood	−896.38		−839.32	
No. of observations	3,874		3,874	
No. of markets	294		294	

Notes. The first column, "Endogenous actions," reports estimates that include only firm-driven outcomes. The second column, "FDA outcomes," includes FDA-determined approvals and rejections (i.e., *Number of competitors exited due to FDA* and *Number of competitors launched*).

One reason for this insignificant effect might be that for the focal firm, the time to its own patent expiry might matter for the decision of *whether* to enter, not *when* to enter, which is what is modeled here. Budish et al. (2015) find evidence for such an effect, where firms invest in diseases where the endpoint is faster to achieve. Other possible reasons include (1) too few observations, which make the estimates noisy (note that the data are available only for the subset of approved drugs), and (2) feasibility of patent extension in this industry. Because firms in this industry know how to extend patents, which is a tactic often used, the actual time remaining may not be a significant factor in deciding whether to continue. I elaborate on these possibilities in Online Appendix C.

Whereas patent life plays an insignificant role in this subset, it might be binding for other drugs. To address both these possibilities, I estimate the model under two assumptions. First, I estimate the model assuming firms get $T = 30$ years to earn profits upon approval. This assumption mimics a world where patent extension is feasible and the time remaining on a drug's patent is not a significant factor in determining investment decisions. Second, I estimate the model assuming firms get $T = 5$ years upon launch. This assumption corresponds to the world where the firm's patent is close to expiry and the current market exclusivity period provided by the FDA binds.

3. Model

3.1. Simple Static Model

Borrowing from the model described in Bresnahan and Reiss (1991a), I first illustrate the main idea of the paper using a simple model containing only two firms, $F1$ and $F2$. Let π^M and π^D denote monopoly and duopoly revenues, respectively, and let c denote the

research cost. Let the market be such that it is lucrative for only one firm, $F1$, to enter; that is,

$$\begin{aligned} \pi^{\mathrm{M}} - c > 0, \\ \pi^{\mathrm{D}} - c < 0. \end{aligned} \tag{1}$$

Now consider the counterfactual, in which incentives are provided such that market size increases by N (e.g., through a faster FDA approval process). Firm $F2$ will enter if

$$N\pi^{D} - c > 0. \tag{2}$$

From the perspective of the focal firm, $F1$, profits drop from $\pi^{M} - c$ to $N\pi^{D} - c$ if $\pi^{M} < N\pi^{D}$. Total market profits, which now equal $2(N\pi^{D} - c)$, will also be lower if $2(N\pi^{D} - c) < \pi^{M} - c$.

Figure 5 plots the probability that the market supports a monopoly, a duopoly, or no firm, for a specific set of parameters and adds an extreme-value error term to each firm's profits. As can be seen, the relationship between the market supporting a monopoly and the market-size factor N is nonmonotone; that is, the focal firm $F1$ benefits from increasing monopolistic profits only up to a certain market size, beyond which profits decline to duopoly levels.

The goal of this paper is to empirically recover the degree of competition in pharmaceutical markets, which will inform policies geared toward increasing market size or subsidizing research costs.

3.2. R&D Investment Model Setup

I now describe the model that governs a firm's decision to enter Phase 3 clinical trials or not and, conditional on entry, to continue investment in these clinical trials, file for an NDA, or exit the market. These decisions are influenced by (1) the structural parameters, which include the cost to enter Phase 3 clinical trials, continuation costs of research, and profitability by market type; (2) the firm's own state; (3) the competitors' states, and (4) privately observed shocks (e.g., adverse side effects in clinical trials can cause the firm to exit). The payoff is positive only if a firm launches its product in the market. Payoffs in the investment stages reflect the cost of continuing research.

Outcomes that are not in the firm's control include approval and rejection by the FDA; that is, once a firm has chosen to file for an NDA, the outcome after this step is determined by the FDA.

I now briefly go over the reasons a firm can exit the market and explain how the model captures these reasons. A firm can exit the market for one of three reasons: (1) adverse effects of the drug on the patient population that are discovered during research, (2) competitive considerations, or (3) FDA rejection after the firm has filed for an NDA.

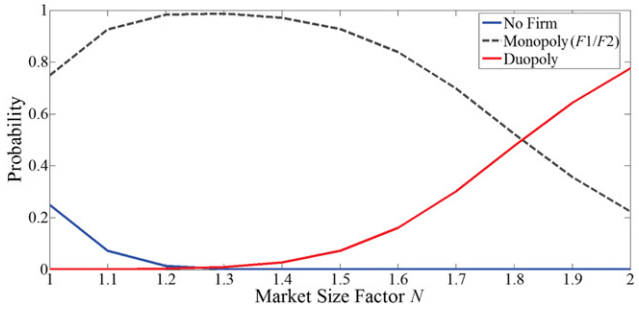
Adverse effects: If a firm's drug has adverse effects on its desired patient population, the firm will have to withdraw testing and exit the market. The error term ε_{ex} present in the utility from exiting the market captures this effect. A large positive shock captures the effect of an adverse event, whereas a negative shock captures the effect of a windfall. Competitors are assumed to know these error shocks only in expectation.

Competitive considerations: This captures a firm's decision to endogenously exit or continue investment in the clinical trials as influenced by its competitors' states and actions. This influence is captured through the state space in the firm's consideration—the extent of this influence is empirically estimated.

FDA rejection: A firm, when it is reasonably confident that it has all the data to justify a launch, submits the relevant documents to the FDA, which then reviews them. On the basis of its review, the FDA may reject the firm's petition to launch in the market. I capture this as a probability, pr_e, associated with exit conditional on filing. These probabilities are directly inferred from the data and conditional on filing are assumed to be exogenous.

3.2.1. States and State Transitions. The state space consists of those variables that are observed to the researcher, x_t, and those that are unobserved to the researcher, s. Both variables are known to the firm $i, i \in \{1, \ldots, I\}$. The unobserved state allows for market-specific heterogeneity. A market's type is assumed to be fixed over time; that is, it cannot transition from one state to another. Markets are assumed to be independent. Firm i's observed state in period t is denoted by x_{it}, where $x \in \{NotEntered, R1, R2, R3, R4, R5, Exit, File, ExitFDA, Launch\}$. Here, *NotEntered* indicates that the firm has not yet entered the market, $R1, \ldots, R5$ denotes the research year[14] the firm is in, *Exit* indicates that the firm has exited the market, *File* indicates that the firm has filed for an NDA and is waiting to hear of an outcome from the FDA, *ExitFDA*

Figure 5. (Color online) No Entry, Monopoly and Duopoly Probabilities as a Function of Market Size



Note. Here, $\pi^{M} = 10, \pi^{D} = 6, c = 8$; $F1/F2$ indicates a monopoly where either $F1$ or $F2$ is the monopolist.

indicates that the FDA rejected the firm's NDA, and *Launch* indicates that the firm won FDA approval. Note that *Exit*, *ExitFDA*, and *Launch* are all absorbing states; that is, once a firm has reached this state, it remains in this state. Further note that although a competitor that has not entered or that has exited does not impact the focal firm's *current* payoffs, these two states have very different implications for the focal firm's *future* payoffs and continual probabilities. In the first state (competitor not entered), there is a potential threat of entry that lowers the focal firm's future profits and hence the probability to enter/continue research; in the second state (competitor exited), the threat is forever eliminated, increasing the focal firm's probability to enter/continue research.

I now describe the state transitions that determine a firm's next-period state given its current state and action.

If a firm has not yet entered Phase 3 in year t, it can choose action d_{it}, where $d \in \{ne,e\} \equiv \{Not\ Enter, Enter\}$. Its next-period state is then given by

$$x_{it+1} = R1 \cdot \mathbb{I}(d_{it} = e) + NotEntered \cdot \mathbb{I}(d_{it} = ne), \quad (3)$$

where $\mathbb{I}(.)$ is the indicator function.

If a firm is an incumbent, it can choose action d_{it}, where $d \in \{c,f,ex\} \equiv \{Continue,File,Exit\}$. Its next-period state is given by

$$x_{it+1} = \begin{cases} R+1 & \text{if } d_{it} = c, \\ File & \text{if } d_{it} = f, \\ Exit & \text{if } d_{it} = ex. \end{cases} \quad (4)$$

Once a firm's state changes to *File*, its next-period state is determined exogenously by the FDA; that is,

$$x_{it+1} = \begin{cases} Launch & \text{with probability } pr_l, \\ ExitFDA & \text{with probability } pr_e, \\ File & \text{with probability } pr_f = 1 - pr_l - pr_e, \end{cases} \quad (5)$$

where pr_l and pr_e are the exogenous launch and exit probabilities respectively, and are directly informed by the data.[15]

A firm's transition conditional on entry into Phase 3 is captured in the schematic shown in Figure 6.

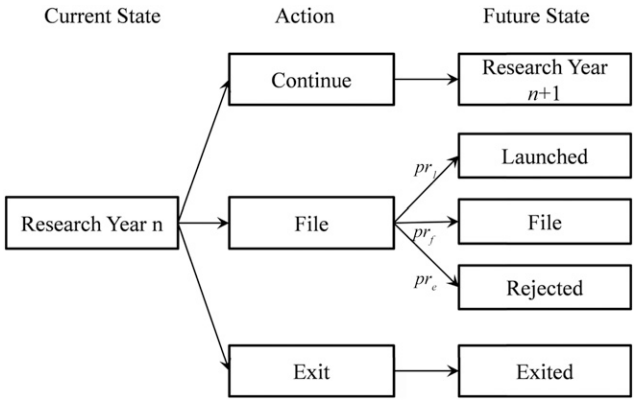
3.2.2. Per-Period Utility. I now specify the current-period payoffs associated with each possible action a firm can take. For an entrant with two possible choices, the per-period utilities of staying out of the market and entering the market are given by Equations (6) and (7), respectively:

$$u_{ne} = 0 + \varepsilon_{ne}. \quad (6)$$

$$u_e = -c_{enter} + \varepsilon_e. \quad (7)$$

where c_{enter} is the cost associated with entering Phase 3.

Figure 6. Schematic of a Firm's Transition from a Research Year to the Next State



For an incumbent with three possible choices, the utility from continuing research, filing for an NDA, and exiting the market are respectively given by Equations (8)–(10):

$$u_c(x_t) = -c_r(x_{it}) + \varepsilon_c \quad (8)$$

$$u_f(x_t) = -c_f(x_{it}) + \varepsilon_f \quad (9)$$

$$u_{ex} = 0 + \varepsilon_{ex}, \quad (10)$$

where $c_r(x_{it})$ is the cost of continuing research and is allowed to depend on firm i's own state. This allows the cost of research to be a flexible function of the firm's investment. The term $c_f(x_{it})$ reflects the likelihood that a firm is more or less likely to file with the FDA when its level of investment is x_{it}. For example, if $c_f(x_{it})$ is decreasing in x_{it}, then the more years a firm spends in research, the more likely it is to file with the FDA. On the other hand, if this function is increasing in x_{it}, the firm is less likely to file with the FDA, reflecting the fact that the firm was not able to garner positive results over the years of research. Firms' final clinical trial outcome is captured through ε_f.[16] The error terms allow drugs with identical states to have different outcomes and success rates (mimicking reality). The error term is interpreted as an unobserved state variable, the exact realization of which is observed only to the agent (Rust 1994). Persistent heterogeneity within a drug, if any, will be infeasible to capture because of the small number of observations per drug.

If the firm has reached the launch phase, it earns profits that are allowed to depend on the number of competitors who are also in the launch stage. I assume the following form of the payoff function:

$$u_l(x_t) = \pi + \delta \sum_{-i} 1(x_{it} = Launch), \quad (11)$$

where $\sum_{-i} 1(x_{it} = Launch)$ is the total number of competing firms in the launched state, π is the profit potential of the market when no competitors are present, and δ is the impact of additional competitors on profits.

This payoff function deviates from the typical payoff used in the literature, which uses product substitutability as revealed by consumer purchase decisions in the marketplace to infer the degree of competition. This is because, unlike most industries, the pharmaceutical industry has a very high failure rate: in the data, only 5.71% of all drugs reach a launch stage. Inferring competition from marketplace substitution is nearly impossible, because one does not observe such substitution for most of the drugs in the data. Moreover, one cannot use characteristic-based models (e.g., Berry and Pakes 2007), using demand data from launched products to infer demand for unlaunched products with similar characteristics. Such inference is infeasible in this setting because a large majority of indications do not have even one launched drug in the span of the data.[17] As a result, I focus on recovering δ, which reveals competitive behavior as inferred from firms' exit decisions in R&D. This functional form allows for different revenues when there is just one firm in the market and when there are multiple firms. However, it is assumed that the first and second additional competitors impact the focal firm's profitability similarly. In Online Appendix F, I relax this assumption allowing the first additional competitor to have a different impact than the second additional competitor. I find that when there are two additional launched firms, the impact is almost twice that of when there is just one additional launched firm, justifying the simple functional form assumption of the competitive impact as δN.

The structural parameters are represented by the vector $\theta = \{c_{enter}, c_r, c_f, \pi, \delta\}$.

3.2.3. Value Functions. The choice-specific value functions if a firm is a potential entrant can be given by the following equations:

$$V_{ne}(x_t, s) = u_{ne} + \beta \sum_{x_{t+1}} \text{Emax}_{\varepsilon'}(V_{ne}(x_{t+1}, s), V_e(x_{t+1}, s)) \cdot f_{ne}(x_{t+1}|x_t), \quad (12)$$

$$V_e(x_t, s) = u_e + \beta \sum_{x_{t+1}} \text{Emax}_{\varepsilon'}\left(V_c(x_{t+1}, s), V_f(x_{t+1}, s), V_{ex}(x_{t+1}, s)\right) \cdot f_e(x_{t+1}|x_t). \quad (13)$$

The summation is over all the possible states (dim $\prod_{-i}|x_{-i,t+1}|$) that all of firm i's competitors can be in, in the next time period.[18] The probability of each of these states occurring is given by $f_j(x_{t+1}|x_t)$ if j was the action i chose in period t. Note that i's own state in the next period can be determined from the state-transition equations described in Equations (3)–(5).

The choice-specific value functions for an incumbent firm is given by the following equations:

$$V_c(x_t, s) = u_c(x_t) + \beta \sum_{x_{t+1}} \text{Emax}_{\varepsilon'}\left(V_c(x_{t+1}, s), V_f(x_{t+1}, s), V_{ex}(x_{t+1}, s)\right) \cdot f_c(x_{t+1}|x_t), \quad (14)$$

$$V_f(x_t, s) = u_f(x_t) + \beta \sum_{x_{t+1}} \left(pr_l \cdot V_l(x_{t+1}, s) + pr_e \cdot V_{exFDA}(x_{t+1}, s) + pr_f \cdot V_{fFDA}(x_{t+1}, s)\right) \cdot f_f(x_{t+1}|x_t), \quad (15)$$

$$V_{ex}(x_t, s) = 0. \quad (16)$$

Once a firm has filed with the FDA, the corresponding value functions are

$$V_l(x_t, s) = u_l(x_t, s) + \beta \sum_{x_{t+1}} V_l(x_{t+1}, s) f_l(x_{t+1}|x_t), \quad (17)$$

$$V_{fFDA}(x_t, s) = 0 + \beta \sum_{x_{t+1}} \left(pr_l \cdot V_l(x_{t+1}, s) + pr_e \cdot V_{exFDA}(x_{t+1}, s) + pr_f \cdot V_{fFDA}(x_{t+1}, s)\right) \cdot f_{fFDA}(x_{t+1}|x_t), \quad (18)$$

$$V_{exFDA}(x_t, s) = 0. \quad (19)$$

Note that although Equations (17)–(19) are subscripted for launch, file, and rejection, they are not choice specific, because the firm does not determine these outcomes.

3.2.4. Equilibrium. Firms are assumed to be symmetric in their actions, and their strategies are assumed to be Markov perfect. A firm chooses the action that maximizes its value function conditional on the current state space and its expectation of other firms' strategies:

$$V(x_t, s|d^*_{it}, d_{-i}) \geq V(x_t, s|d'_{it}, d_{-i}). \quad (20)$$

4. Estimation

The parameters are recovered using the EM algorithm described in Arcidiacono and Miller (2011). The estimation recovers (1) the probability q_{ms} that market m belongs to type s, (2) the overall population probability of the unobserved states π_s, (3) the type-specific conditional choice probabilities (CCPs) as a function of observed states, and (4) the type-specific structural parameters θ. The discount factor, β, is assumed to be 0.9.

In Online Appendix E, these parameters are recovered by therapeutic area (i.e., assuming type s is observed).

I first specify the likelihood of the data and how to obtain the CCPs from the data, and then I list the steps used in estimation. To ease the computational burden, if a market contains more than four incumbents, I use only the first four firms that entered the market.

4.1. Likelihood

Assuming the ε's are independent and identically distributed and follow a Type I extreme-value distribution, the choice-specific value functions for an incumbent can be written as

$$v_c(x_t,s;\theta) = -c_r(x_{it}) + \beta \sum_{x_{t+1}} \left(\Gamma + \ln\left[e^{v_c(x_t,s;\theta)} + e^{v_f(x_t,s;\theta)} + e^{v_{ex}(x_t,s;\theta)}\right]\right) \cdot f_c(x_{t+1}|x_t), \tag{21}$$

$$v_f(x_t,s;\theta) = -c_f(x_{it}) + \beta \sum_{x_{t+1}} \left(pr_l \cdot V_l(x_{t+1},s;\theta) + pr_e \cdot V_{exFDA}(x_{t+1},s;\theta) + pr_f \cdot V_{fFDA}(x_{t+1},s;\theta)\right) \cdot f_f(x_{t+1}|x_t), \tag{22}$$

$$v_{ex}(x_t,s;\theta) = 0, \tag{23}$$

where $v(.) = V(.) - \varepsilon$, and Γ is the Euler function.

Equation (21) can be further simplified by using the fact that exiting the market is a terminal action:

$$v_c(x_t,s;\theta) = -c_r(x_{it}) + \beta \sum_{x_{t+1}} \left(\Gamma + \ln \frac{\left[e^{v_{ex}(x_t,s;\theta)}\right]}{p_{ex}(x_{t+1},s;\theta)}\right) \cdot f_c(x_{t+1}|x_t), \tag{24}$$

where

$$p_{ex}(x_t,s;\theta) = \frac{e^{v_{ex}(x_t,s;\theta)}}{e^{v_c(x_t,s;\theta)} + e^{v_f(x_t,s;\theta)} + e^{v_{ex}(x_t,s;\theta)}}. \tag{25}$$

But $p_{ex}(x_t,s;\theta)$ is the CCP of exiting the market and can be estimated directly from the data. Replacing $p_{ex}(x_t,s;\theta)$ with $\hat{p}_{ex}(x_t,s)$, Equation (24) simplifies to

$$v_c(x_t,s;\hat{p},\theta) = -c_r(x_{it}) + \beta \sum_{x_{t+1}} \left(\Gamma - \ln\left(\hat{p}_{ex}(x_{t+1},s)\right)\right) \cdot f_c(x_{t+1}|x_t), \tag{26}$$

which requires computation of only one-period-ahead CCPs. This idea has been illustrated in Hotz and Miller (1993). Arcidiacono and Ellickson (2011) provide a review of empirical applications that use this simplification, along with detailed derivations.

Note the same simplification cannot be applied to $v_f(x_t,s;\theta)$, because once the firm has filed with the FDA, it no longer has a choice to make—the FDA makes all further decisions. Thus, to compute $v_f(x_t,s;\hat{p},\theta)$, I simulate out V_l and V_{fFDA} using $\hat{p}$ for T time periods. Note that a further simplification can be made when the value function is linear in θ (Bajari et al. 2007). For a given state vector and CCPs, firm actions can be forward simulated. Once any given firm has filed, whether it receives an approval or rejection by the FDA is simulated by drawing probabilities from a uniform distribution NS times. In Equations (27) and (28), terms $1(\text{Launch}_i)$ and $\sum_{-i} 1(\text{Launch}_i)$ are precomputed prior to the maximization step, resulting in value functions linear in π and δ:

$$V_l(x_{t+1},s;\theta) = \sum_{t=0}^{T} \beta^t \left(\pi + \delta \sum_{-i} 1(Launch_i)\right), \tag{27}$$

$$V_{fFDA}(x_{t+1},s;\theta) = \sum_{t=0}^{T} \beta^t \left(\pi.1(Launch_i) + \delta \sum_{-i} 1(Launch_i)\right). \tag{28}$$

The choice-specific value functions for an entrant can be written as

$$v_e(x_t,s;\hat{p},\theta) = -c_{enter} + \beta \sum_{x_{t+1}} \left(\Gamma - \ln\left(\hat{p}_{ex}(x_{t+1},s)\right)\right) \cdot f_e(x_{t+1}|x_t), \tag{29}$$

$$\begin{aligned} v_{ne}(x_t,s;\hat{p},\theta) &= 0 + \beta \sum_{x_{t+1}} \left(\Gamma + \ln\left[\exp(v_e(x_{t+1},s;\theta)) + \exp(v_{ne}(x_{t+1},s;\theta))\right]\right) \cdot f_{ne}(x_{t+1}|x_t) \\ &= \beta \sum_{x_{t+1}} \left(\Gamma + \ln \frac{\left[\exp(v_e(x_{t+1},s;\theta))\right]}{p_e(x_{t+1},s;\theta)}\right) \cdot f_{ne}(x_{t+1}|x_t) \\ &= \beta \sum_{x_{t+1}} \left(\Gamma + v_e(x_{t+1},s;\theta) - \ln\left(p_e(x_{t+1},s;\theta)\right)\right) \cdot f_{ne}(x_{t+1}|x_t) \\ &= \beta \sum_{x_{t+1}} \left(\Gamma - c_{enter} + \beta \sum_{x_{t+2}} \left(\Gamma - \ln\left(\hat{p}_{ex}(x_{t+2},s)\right)\right) \cdot f_e(x_{t+2}|x_{t+1}) - \ln\left(p_e(x_{t+1},s;\theta)\right)\right) \cdot f_{ne}(x_{t+1}|x_t), \end{aligned} \tag{30}$$

which requires evaluation of two-period-ahead CCPs.

The likelihoods of the data for an incumbent and an entrant are given by Equations (31) and (32), respectively:

$$l_{imts}(y_{imt}|x_t,s;\hat{p},\theta) = \frac{\exp(v_c(x_t,s;\theta)) \cdot 1(y_{imt}=c) + \exp(v_f(x_t,s;\theta)) \cdot 1(y_{imt}=f) + 1 \cdot 1(y_{imt}=ex)}{\exp(v_c(x_t,s;\theta)) + \exp(v_f(x_t,s;\theta)) + 1}, \tag{31}$$

$$l_{imts}(y_{imt}|x_t,s;\hat{p},\theta) = \frac{\exp(v_e(x_t,s;\theta)) \cdot 1(y_{imt}=e) + \exp(v_{ne}(x_t,s;\theta)) \cdot 1(y_{imt}=ne)}{\exp(v_e(x_t,s;\theta)) + \exp(v_{ne}(x_t,s;\theta))}, \tag{32}$$

where y_{imt} is the action taken by firm i in market m at time t.

Aggregating across all firms and years, the likelihood of market m of unobserved type s is given by

$$l_{ms}(y_m|x,s;\hat{p},\theta) = \prod_{i=1}^{I} \prod_{t=1}^{T} l_{imts}(y_{imt}|x_t,s;\hat{p},\theta).$$

Aggregating across all types and markets, the log-likelihood of the data is

$$l(y|x;\hat{p},\theta) = \sum_{m=1}^{M}\sum_{s=1}^{S} q_{ms}\ln\left(l_{ms}(y_m|x,s;\hat{p},\theta)\right), \quad (33)$$

where q_{ms} is the probability that market m is of type s.

4.2. CCP Estimation

To get the CCPs, $\hat{p}$, I use a parametric approximation. Let θ_{CCP} denote the parameter vector describing the CCPs. For incumbents, I estimate a logit on the probabilities of continuing, filing, and exiting the market, and for entrants, I estimate a logit on the probabilities of entering and not entering; q_{ms} are used as weights in the logit likelihood.

The continuation function is specified as a linear combination of $(1, \sum_{-i}(x_{-it}=Launch), \sum_{-i}(x_{-it}=Exit), \sum_{-i}(x_{-it}\in\{R1,\ldots,R5\}), \sum_{-i}(x_{-it}=File), \sum_{-i}(x_{-it}=ExitFDA), \sum_{-i}(x_{-it}=Launch), x_{it})$. The function for the entry choice probabilities is specified as a linear combination of $(1, \sum_{-i}(x_{-it}=Launch), \sum_{-i}(x_{-it}=Exit), \sum_{-i}(x_{-it}\in\{R1,\ldots,R5\}), \sum_{-i}(x_{-it}=File), \sum_{-i}(x_{-it}=ExitFDA))$.

4.3. EM Algorithm

I operationalize the EM algorithm with starting values $\pi_s^1, \theta_{CCP}^1, \theta^1$, where the superscript denotes the lth iteration of the EM algorithm. Following Arcidiacono and Miller (2011), I update $q_{ms}, \pi_s, \theta_{CCP}, \theta$ as follows:

1. $q_{ms}^{l+1} = \frac{\pi_s^l l_{ms}(y_m|x,s;\theta_{CCP}^l,\theta^l)}{\sum_{s=1}^{S}\pi_s^l l_{ms}}$.
2. $\pi_s^{l+1} = \frac{\sum_{m=1}^{M} q_{ms}^{l+1}}{M}$.
3. Obtain θ_{CCP}^{l+1} using the specification in Section 4.2 and q_{ms}^{l+1} as weights.
4. $\theta^{l+1} = \text{argmax}_\theta \sum_{m=1}^{M}\sum_{s=1}^{S} q_{ms}^{l+1}\ln(l_{ms}(y_m|x,s;\theta_{CCP}^{l+1},\theta))$.

These steps are repeated until $|\pi^{l+1} - \pi^l| < tol$.

4.4. Identification

Here, I briefly go over the identification of the second-stage parameters $\theta = [c_{enter}, c_r, c_f, \pi, \delta]$. Pesendorfer and Schmidt-Dengler (2008) study identification in the context of dynamic games. In their simple illustrative entry/exit model, firms decide whether to enter, to remain active, or to exit. The state space includes whether the firm was active in the previous period, $s_i = 2$, or not, $s_i = 1$. Specifically, from the payoff function shown in Table 6, they can identify π^1 and c. Observing a firm's action when the second player is active allows them to identify the duopoly profits π^2. Here, $a_i = 0, s_i = 1$ describes a potential entrant that has not yet entered; $a_i = 1, s_i = 1$ describes a potential entrant that has just entered; $a_i = 0, s_i = 2$ describes an incumbent that has exited; and $a_i = 1, s_i = 2$ pertains to an active incumbent.

The model in this paper is an extension of their entry/exit model with one main difference: a firm's action does not directly translate into current-period profits; a firm can only earn profits if it wins FDA approval. After filing, a firm does not take any action but is passively awaiting FDA approval. The payoff matrix can then be written as shown in Table 7, where $a_i = 2$ denotes the action of filing. Note that once a firm has filed, it has no further action to take. In an abuse of notation, I have included the future-term profits in the payoff from filing. However, this feature is important—the net present value of profits always enters the payoff from filing in the same form irrespective of the state space.[19] The only change is when an additional competitor has launched, but this helps identify the competitive impact parameter or duopoly profits. From this payoff matrix, similar to Pesendorfer and Schmidt-Dengler (2008), the observed rate of entry identifies the entry cost c_e, and the continuation rate identifies the cost of research c_r relative to the cost of exiting. In addition, the observed filing rate identifies the net of cost of filing c_f and profits π^1. One cannot separately identify the two.[20] I therefore normalize filing costs to 0 because filing with the FDA is costless for a firm.[21] The competitive impact parameter δ is identified based on firms' responses to launched competitors. If we observe more exits when more launched competitors are present, it implies a negative effect of competition on revenues.

5. Results

5.1. Estimation Details

In this section, I report the results under the assumption that firms get $T = 30$ years upon approval (i.e., patent life is not binding and patent extension is feasible). Online Appendix D reports the estimates under the assumption $T = 5$ years. The results are qualitatively similar.

In estimation, I use a parsimonious model as well as a model that includes market and year fixed effects in the first and second stages of the model. I do so because including market and year fixed effects makes the entry CCP estimates close to that recovered in the reduced form (Table 5).[22] In the second stage of Specification (2), I allow for a different entry cost parameter for each market and each year. I also allow for a different research cost parameter for each therapeutic area (it is infeasible to estimate research costs at the market level) and each year. Such a structural model will have entry and continuation CCPs that differ for each market and year. Ideally, the CCPs would be estimated market by market and year by year, but data sparsity prevents such a flexible specification. The assumption is that fixed effects in the CCPs are sufficient to absorb this variation.

Table 6. Payoffs in a Standard Entry/Exit Model

	$s_i = 1$	$s_i = 2$
$a_i = 0$	0	x
$a_i = 1$	$\pi^1 + c$	π^1

Table 7. Payoffs Including the Decision to File

	$s_i = 1$	$s_i = 2$
$a_i = 0$	0	x
$a_i = 1$	c_e	c_r
$a_i = 2$	N/A	$c_f + \pi^1 f(pr_l)$

I recover two (unobserved) types of markets using the EM algorithm. Each disease market is a mixture of the two latent types recovered. In Specification (1), the percentage of type 1 markets from the estimation is 4%, which implies that the average disease market is 4% type 1 and 96% type 2. Across all markets, the percentage that a market is type 1 varies from 0.7% to 11.94%. Even though 96% of markets are type 2, allowing for two types leads to a better fit relative to allowing for only one type. The log likelihood of a two-type model is 2,471.0 and for a one-type model is 2,495.57. The likelihood ratio test statistic $2(LL_{\text{two-type}} - LL_{\text{one-type}}) = 49.14$ is greater than $\chi^2(26, 0.05) = 38.8$. This test supports the two-type model, which has an additional 26 parameters, at a significance level of 0.05. In Specification (2), the test supports the one-type model, likely because of the large number of fixed effects included. However, I include two types in this specification because it helps recover important aspects of heterogeneity that otherwise get attenuated in a homogeneous model.

5.2. CCP Estimates

The CCP estimates, θ_{CCP}, for continuation and filing for incumbents, and entering for entrants, are shown by type of market in Table 8. The signs of both the continuation and entry CCPs, in Specification (2), are in line with the reduced-form estimates. Overall, these estimates indicate competition has a negative effect on a firm's continuation decisions. On average, the focal firm is less likely to continue when a competitor has launched or is in research, and it is more likely to continue when a competitor has exited the market or has received an FDA rejection. The focal firm is also less likely to enter when a competitor has launched or is in research.

However, the likelihood of entry decreases when competitors exit. This can occur because data restrictions imply that we do not always see outcomes over the entire state space. For example, we might always see more exits accompanied with more launches. If this is the case, the reduced form will provide inconsistent estimates. Second, from a statistical perspective, there is a chance that one parameter has a wrong sign. This is more likely in the first stage where there are many estimates. However, the hope is that other states are informative of competitive conduct, and we accurately estimate the competitive parameter, which is the object of interest.

5.3. Structural Estimates

Table 9 presents the structural parameter estimates θ. Research costs in Specification (1), which does not include fixed effects, are positive, suggesting continuing research is costly. In this specification, the net payoff from entering Phase 3 is positive, implying that firms have incentives to enter even when the market may not support such entry. This higher rate of entry might occur if there is an immediate payoff from stock market/shareholder response upon seeing an advancement in the firm's pipeline.[23]

The monopoly yearly revenue for type 2 markets is about half the cost of doing research in year 1. Upon launching, with 20 years remaining, a monopolist would earn 1.437 utils of revenue. The main parameter of interest, δ, is significantly negative for type 2 markets. The value of δ relative to π indicates most markets support at most two launched firms.

Estimates in Specification (2) largely echo these findings. Note the reported research costs cannot be interpreted directly, because research costs are a sum of these common research costs and the (unreported) market and year fixed effects in the decision to continue.[24]

The mixture of types can be used to roughly compute the average number of firms each disease market supports. I compute the weighted average of π and δ for each of the 294 disease markets as $\pi_m = \sum_s q_{ms}\pi_s$ and $\delta_m = \sum_s q_{ms}\delta_s$. The resulting market-specific π_m and δ_m can be used to compute the estimated number of firms each market can support as $\hat{N}_m = \frac{\pi_m}{\delta_m}$. I then regress this estimated number on the actual number of firms, N, from the data. For Specification (1), the estimated coefficient is 1.13 and is statistically significant (t-statistic = 6.1), and for Specification (2), the estimate is 1.28 (t-statistic = 4.23), indicating that the mixture allows different markets to support different numbers of firms. Moreover, this coefficient is statistically not different from 1, indicating that the structural model predicts the data well, providing a validation check. Figure 7 plots the relationship between the estimated (using estimates from Specification (2)) and true N per market. Having just one type would restrict all markets to have the same δ and π, which would not represent the heterogeneity present across all markets.

In Online Appendix E, where I estimate the model by therapeutic area, I find a similar effect of competition. Although a lack of sufficient observations per therapeutic

Table 8. CCP Estimates: θ_{CCP}

	Specification (1)				Specification (2)			
	Type 1		Type 2		Type 1		Type 2	
	Coefficient	*t*-statistic	Coefficient	*t*-statistic	Coefficient	*t*-statistic	Coefficient	*t*-statistic
Incumbent (base outcome: exit)								
Continue								
Constant	1.76	2.14	4.13	21.79	4.42	15.06	5.81	6.70
Number of competitors launched	–0.04	–0.03	–0.28	–2.03	–0.20	–1.53	–3.08	–5.18
Number of competitors exited	0.30	0.23	0.11	0.75	0.32	1.95	6.04	289.05
Number of competitors in research	–1.53	–1.06	–0.22	–2.24	–0.33	–3.49	–0.16	–0.24
Number of competitors in filed status	–1.69	–1.52	0.32	1.47	0.41	1.72	2.32	33.47
Number of competitors exited due to FDA	1.62	2.66	0.64	3.43	1.09	6.44	—	N/A
Own state: Research Year 1	1.40	2.04	–1.66	–9.76	–1.28	–6.84	3.35	138.92
Own state: Research Year 2	–0.53	–0.73	–1.64	–8.65	–1.24	–6.47	3.77	101.86
Own state: Research Year 3	–5.61	–7.52	–1.29	–6.23	–1.11	–4.17	3.30	71.14
Own state: Research Year 4	–1.76	–1.54	–1.00	–3.97	–0.77	–3.62	–0.93	–1.48
File								
Constant	2.02	1.87	0.34	2.53	0.44	4.94	–1.58	–1.94
Entrant (base outcome: not enter)								
Enter								
Constant	–1.72	–6.79	–1.98	–40.28	–5.21	–14.57	–5.07	–13.36
Number of competitors launched	0.44	0.46	0.65	5.48	–2.86	–6.25	–0.08	–5.25
Number of competitors exited	1.73	2.15	0.65	4.21	–1.58	–3.83	–2.42	–8.61
Number of competitors in research	0.46	0.84	0.53	5.51	–1.24	–6.50	–1.77	–5.52
Number of competitors in filed status	–0.68	–0.61	0.08	0.37	–2.46	–5.95	—	N/A
Number of competitors exited due to FDA	0.18	0.55	0.05	0.16	–3.61	–5.26	—	N/A
Fixed effects	No				Yes			
% type *m*	4.08		95.92		89.6		10.4	
Number of markets	294				294			

Notes. Standard errors are computed using bootstrap with replacement over 40 draws. Specification (1) has no fixed effects. Specification (2) has year and market fixed effects (unreported) in both the first and second stages of the entry and continuation models. (—, N/A): insufficient data to estimate parameter.

area makes meaningful statistical inference difficult, the sign of the competitive impact parameter for 16 of the 19 therapeutic areas where estimation is feasible is negative. In Online Appendix F, I also provide estimates from a more flexible profit function, which allows the first firm to have a different impact than the second firm.

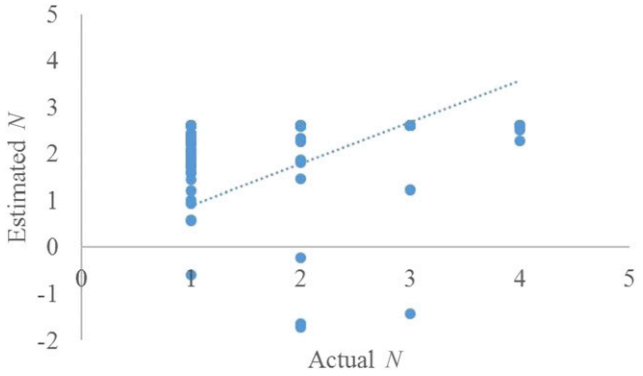
The FDA approval probabilities (Table 10) are recovered directly from the data. Conditional on being

Table 9. Structural Parameter Estimates: θ

		Specification (1)				Specification (2)			
		Type 1		Type 2		Type 1		Type 2	
Parameter	Symbol	Coefficient	*t*-statistic	Coefficient	*t*-statistic	Coefficient	*t*-statistic	Coefficient	*t*-statistic
Entry payoff	c_{enter}	–1.89	–0.92	–0.95	–3.39				
Research cost (Year 1)	c_{r1}	–0.04	–0.02	0.43	2.82	–0.14	–0.62	–0.49	–7.72
Research cost (Year 2)	c_{r2}	1.63	1.83	0.68	4.35	–0.03	–0.10	–1.14	–11.87
Research cost (Year 3)	c_{r3}	8.70	5.73	0.56	2.98	0.07	0.20	–4.20	–33.50
Research cost (Year 4)	c_{r4}	11.29	10.03	1.10	4.47	0.34	0.99	0.35	0.31
Research cost (Year 5)	c_{r5}	—	N/A	0.11	2.56	–0.43	–1.77	–0.51	–0.33
Revenue	π	–0.32	–0.08	0.18	3.25	0.22	4.52	–1.00	–1.50
Competitive impact	δ	0.80	0.26	–0.10	–1.93	–0.09	–1.99	0.07	0.20
Fixed effects		No				Yes			
% type *m*		4.08%	2.70			89.6%	91.96		

Notes. Standard errors are computed using bootstrap with replacement over 40 draws. Specification (1) has no fixed effects. Specification (2) has year and market fixed effects (unreported) in both the first and second stages of the entry and continuation models. (—, N/A): insufficient data to estimate parameter.

Figure 7. (Color online) Plot of Estimated N vs. Actual N



Note. Slope of the line is close to 1.

in review, a firm has a 26.2% chance of receiving approval, a 71.6% chance of remaining in review, and a 2.3% chance of receiving rejection.

I next simulate out the equilibrium responses of firms for $T = 50$ periods using the structural estimates and the model in Section 3. I do this to (1) compare the simulation outcome to the data, providing a validation check, and (2) evaluate the impact of competitors on a firm's payoff conditional on launching. The equilibrium I consider is Markov perfect, where firms' strategies depend only on the current state variables. In equilibrium, each firm behaves optimally and has rational expectations about competitors' actions. To solve for the equilibrium, I backward simulate the dynamic game starting at $T = 50$. Each period, I solve for the equilibrium at each possible state. Upon launch, and in line with the estimation model, firms get 30 years to participate in the market after which revenues drop to zero.

To make meaningful comparisons between the data and simulations, I perform the validation exercise using type 2 market estimates from Specification (1). The absence of fixed effects in this specification implies that I do not have to solve the model for every market separately. Moreover, I can pool across markets in the data getting meaningful probabilities, whereas focusing on one market can result in sparse values at any given state. Table 11 provides a validation check on *Entry*, *Exit*, and *File* probabilities when no other player has entered the market. The *Exit* and *File* probabilities are averaged over all possible research states to allow for sufficient observations. In Table 11, N is the total number of observations in the data that satisfy the relevant criteria. The model appears to replicate the data reasonably well.

Table 10. FDA Approval Probabilities Conditional on Firm's Filing for an NDA

	Probability of...		
	Remaining in review	Approval	Rejection
	pr_f	pr_l	pr_e
Current FDA (%)	71.60	26.20	2.30

Table 11. Validation Check

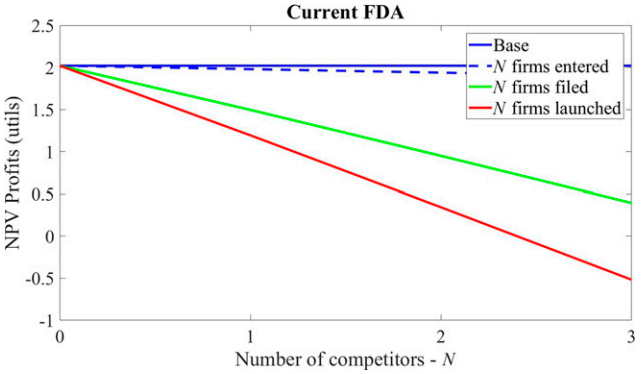
	N	Data (%)	Simulation (%)
Pr(*Entry*)	263	13.5	11.6
Pr(*Exit*) (from research)	35	3.4	4.2
Pr(*File*) (from research)	77	7.8	9.7

Note. No competitor has entered the market.

5.4. Impact of Competition on Expected Profits

In Figure 8, I plot the value function conditional on launching as a function of competitors' states. For this computation and for all counterfactuals, I simulate the equilibrium using type 1 market estimates from Specification (2). Each line represents the value function evaluated at four different states; the baseline is the value when no other firm has entered R&D. The dotted line plots the value when 0, 1, 2, or 3 of the firm's competitors have entered Phase 3. This line shows that as the number of competitors that have entered Phase 3 increases, the NPV of profits decreases, but not by much, because firms know that after entry, the competitor still has many years remaining before it might launch in the market. However, if the competitor has filed, there is a 26.2% probability that it will get approved, and this causes the NPV to decline further. Finally, as the number of competitors that have launched increases, profits decline the most. Figure 8 also shows that the NPV of profits becomes negative when the number of competitors reaches three, implying that the market does not support more than two firms.

Figure 8. (Color online) Impact of Competition on Profits Conditional on Launching



6. Counterfactual Policy Evaluations

6.1. Effect of a Faster FDA Approval Process

To measure the impact of a faster FDA approval process, I modify the FDA's probability of approval so that the time in review is reduced, holding fixed the total number of approvals. Table 12 presents the current FDA probabilities as well as the probabilities used in this counterfactual evaluation, and Figure 9 plots these probabilities over time. In the data, the probability of a firm staying in review is 71.6%, whereas in the counterfactual, I reduce this to 31.6%. I adjust the per-period approval probability to 62.9% to ensure that overall approval and rejection probabilities are the same over a span of 20 years; that is,

$$\sum_{t=1}^{T} pr_f^{t-1} \cdot pr_l = \sum_{t=1}^{T} pr_{f,faster}^{t-1} \cdot pr_{l,faster},$$

where $pr_{f,faster}$ is the in-review probability in the counterfactual of a faster FDA approval.

I then recompute the new equilibrium under the counterfactual of a faster approval process. The appendix presents the algorithm for computing the equilibrium. For all counterfactuals, I simulate the equilibrium using type 1 market estimates from Specification (2). For the sake of illustration, I restrict attention to the therapeutic area trauma (to determine research costs) and the market schizoaffective disorders, which is categorized under this therapeutic area (for entry costs). The respective research and entry costs are 0.43 and 23.48. For year fixed effects, I take the average estimated value across the 12 estimates for the 12 years, resulting in an average yearly entry cost of −23.13. The qualitative nature of the results holds under various other specifications tried (including using zero research and entry costs, fixed effects from a market with lower entry costs, and estimates from Specification (1)): only the absolute levels of the probabilities change.

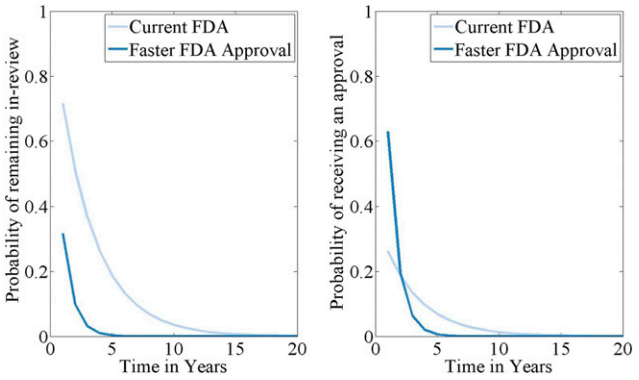
6.1.1. Expedited Review Increases Competitive Intensity.

I first evaluate the NPV of profits for a firm that has just launched. Because the speediness of the approval process does not directly impact the launched firm (it has already received approval), any difference in NPV arises from the extent to which its competitors are impacted by the expedited review. This exercise therefore helps evaluate the impact coming solely from strategic considerations. I also assume that upon launch, a firm has 30 years to enjoy its profits. Figure 10 plots the value function conditional on a launch. In the counterfactual of a faster FDA process, the NPV conditional on a launch is lower and declines much more rapidly as the competitor gets closer to a launch. The decline occurs because, unlike in the current FDA, competitors remain in review for shorter periods of time, which in turn reduces the launched firm's term as a monopolist. Ching (2010a) documents a similar effect in the generics market.

Table 12. FDA Approval Probabilities Conditional on Firm Filing for an NDA

	Probability of...		
	Remaining in review (%)	Approval (%)	Rejection (%)
Current FDA	71.60	26.20	2.30
Faster FDA Approval	31.60	62.99	5.41

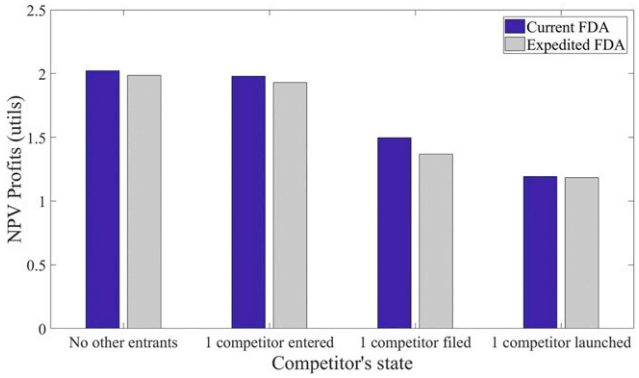
Figure 9. (Color online) Ex Ante Probabilities of Remaining In Review and Approval



6.1.2. Expedited Review Encourages Innovation.

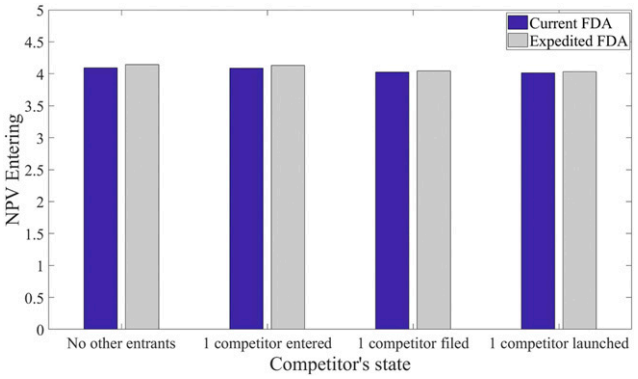
The NPV of profits, conditional on a launch, is informative of the increased competitive intensity firms face once in the market under an expedited FDA. However, this does not inform us of the degree to which an expedited review process is beneficial. To see whether the lower NPV of profits outweighs the quicker access to these profits, one needs to look at the value of entry. To this end, I plot the value function of entering R&D (Figure 11), as well as the probability of entering

Figure 10. (Color online) Impact of Competition on Profits—Faster FDA Approval Reduces NPV of Profits



Note. Other two competitors have not entered.

Figure 11. (Color online) Value Function of Entering as a Function of Competitor's States—Faster FDA Approval Encourages Entry



Note. Other two competitors have not entered.

(Figure 12), as a function of the number of competitors who have entered the research process. Clearly, these figures show that quicker access to the market outweighs the loss from having a more competitive market. This is true as long as fewer than three firms have filed or launched, because the market does not support more than three launched firms.

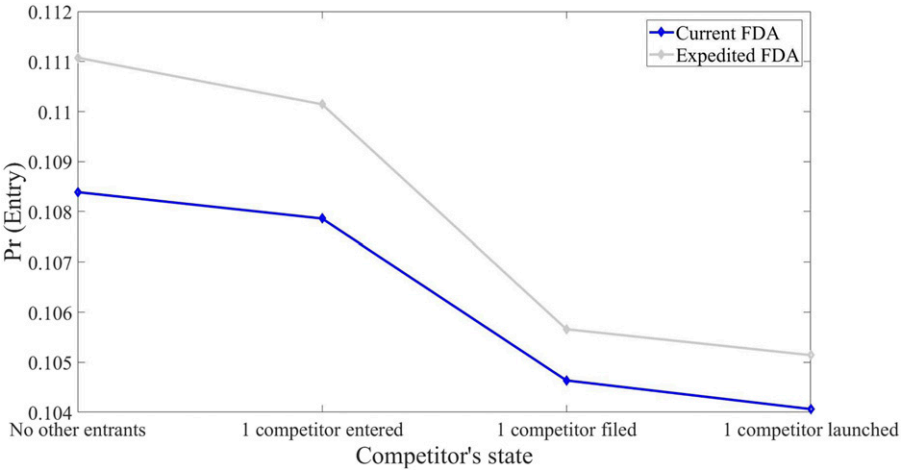
6.1.3. Negative Impact of an Expedited Review Process?.

The high degree of uncertainty of the pharmaceutical R&D process implies that the first firm to enter R&D need not be the first to launch. A late entrant that receives a positive draw in the research process can reach the market first. In such a case, the probability is higher that the early entrants (incumbents) exit the R&D process. Figure 13 plots the exit rates as a function of the firm's competitor, when two competitors have already launched. The exit probability of the incumbent increases if the competitor files or launches, which is cause for concern surrounding wasteful investment. To see whether this increased exit rate is economically significant, I quantify the R&D dollars that might have been unnecessarily spent. The additional increase in exit rate, when two competitors have filed and the other has not entered, is 0.0001. Assuming Phase 3 R&D costs per firm of \$200 million[25] implies a wasteful investment of \$0.02 million. This amount is fairly insignificant given (1) the high R&D costs firms incur and (2) the potential benefits to consumers of having more entrants vie for entry into the marketplace.

6.1.4. Quantifying the Effects: Competitive Intensity vs. Reduced Time to Market.

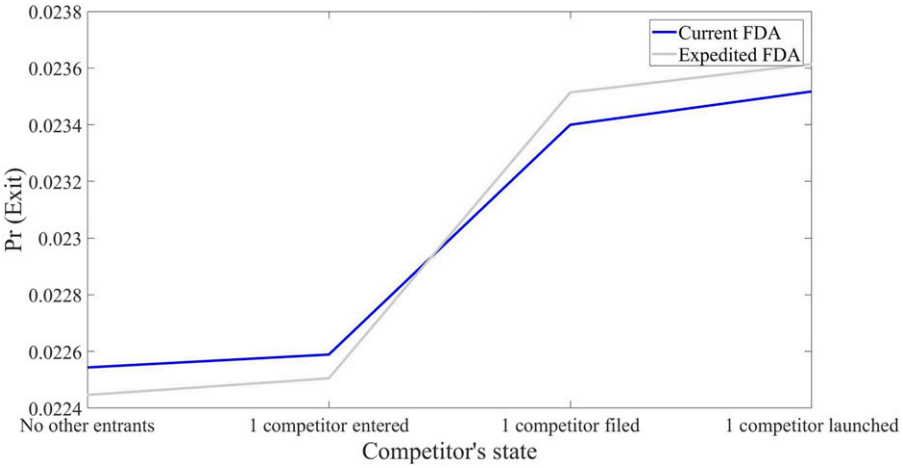
To quantify the extent to which each effect dominates, I compare the value functions solved by computing the dynamic equilibrium under a faster FDA approval process to the value functions if firms acted without any strategic behavior (i.e., ignored the states of their competitors).[26] Figure 14 plots the entry value functions, v_e, under the two scenarios along with the base-case scenario of the current approval process. The state space chosen is such that the firm's competitors are far from launching (no one else has entered). As can be seen, the focal firm benefits from an expedited approval process: the value from entering is 1.17% higher than in the current FDA approval process. In other words, the benefit from the reduced time to market outweighs the competitive effects. Note that in a world where patent life is more binding, an expedited approval provides the added benefit of longer time remaining on a firm's patent. The bias, if firms did not consider their competitors' strategic responses, is 1.27%.

Figure 12. (Color online) Entry Probability as a Function of Competitor's States—Firm Is More Likely to Enter Under Expedited Approval



Note. Other two competitors have not entered.

Figure 13. (Color online) Exit Probability as a Function of Competitor's States—Higher Exit Rates When Competitors Are Closer to Launch



Note. Two competitors launched.

Next, I repeat the same exercise but for when the firm's competitors are close to launch (three competitors have filed). Figure 15 shows that the focal firm is worse off under an expedited approval process, because competitive effects outweigh any potential gain from a faster approval process. Compared with the current regime, the focal firm's access to monopoly profits is lower when competitors are likely to get an approval soon. Moreover, when competitors' states are not accounted for, one can misleadingly conclude a large positive impact of an expedited FDA process.

6.2. Increased Market Exclusivity

To evaluate the impact of longer market exclusivity, I extend the current FDA-granted exclusivity by one year. To realistically simulate this, I use the model estimates where firms get five years upon launch, reported in Online Appendix D. I do not use the model estimates where firms get 30 years upon launch because that implies a long remaining patent life, and an extension in exclusivity by one year will have little perceptible impact.

Figure 16 plots entry probabilities under the current exclusivity period (5 years), expedited approval (5 years), and increased exclusivity (6 years). Although increased exclusivity increases the probability of entry, this increase is lesser than when the approval process is faster. An early approval provides a larger incentive for firms because firms can begin earning profits sooner: the competitive intensity is outweighed by the quicker access to the market, as shown in Figures 11 and 12. However, conditional on a launch, increased market exclusivity benefits the focal firm (Figure 17). This is because, under increased exclusivity, the firm gets an additional year to earn profits. However, under an expedited approval, a launched firm is under the threat that its competitors will soon get an approval limiting its time as a monopolist.

From the focal firm's perspective (that would otherwise have been the only player), an expedited

Figure 14. (Color online) Reduced Time to Market Dominates When Competitors Are Far from Launch

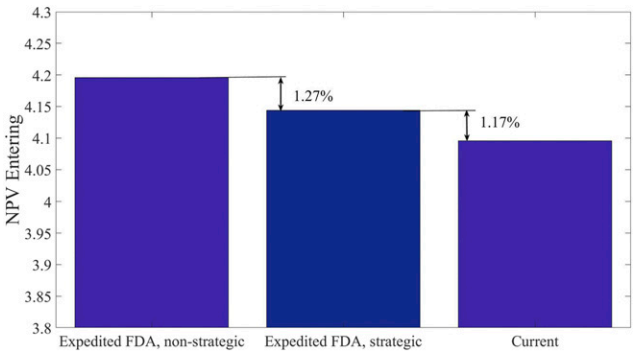


Figure 15. (Color online) Competitive Effects Dominate When Competitors Are Close to Launch

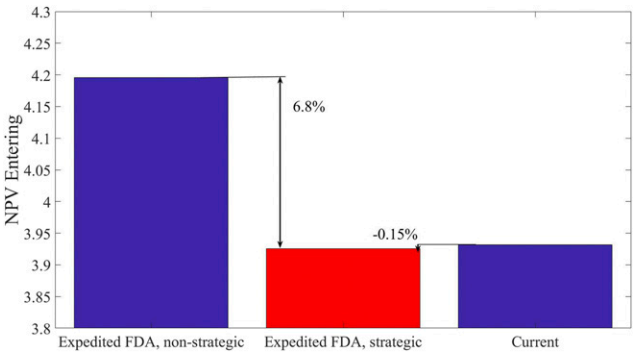
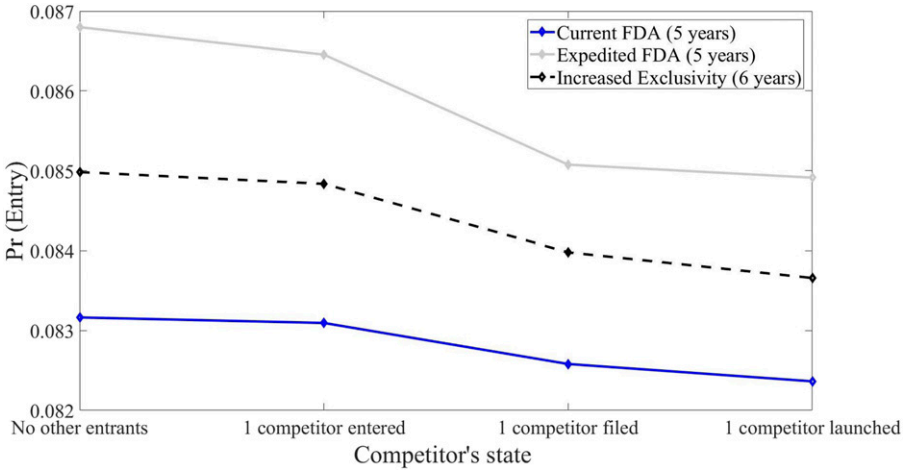


Figure 16. (Color online) Entry Probability: Firm Is More Likely to Enter Under Longer Exclusivity but Less Likely Than Faster Approval



Note. The other two competitors have not entered.

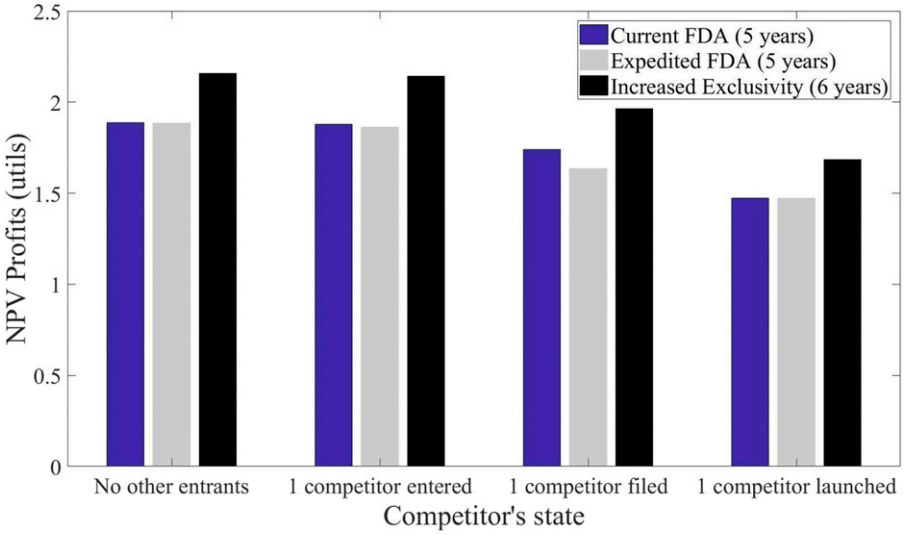
approval intensifies competition and leads to lower profits. However, from a new entrant's perspective (that would otherwise not have participated in the market), an expedited approval renders it a viable player. Market exclusivity, on the other hand, increases profits for the focal firm conditional on a launch, but because these profits are further into the future, the overall entry rates are not as high.

7. Conclusion

This paper finds that a faster FDA process, something pharmaceutical firms are pushing for, is largely beneficial to firms and could also encourage innovation. Although firms face increased competition in this scenario, they benefit from the quicker access to profits. This paper also finds that ignoring strategic considerations can lead one to overestimate the value of entry, which can be especially misleading when the firms' competitors are close to launching. Using a data set on Phase 3 clinical trial entry, continuation, and filing decisions, and FDA outcomes at the firm-market-year level, a dynamic model of oligopoly was estimated accounting for unobserved heterogeneity in markets. This paper finds evidence—both model-free and from the structural parameters—that competition has a negative impact on firms' continuation decisions in R&D.

This paper focused only on the Phase 3 stage of R&D. Acquiring data on the earlier phases of research can shed further light on the dynamics that occur

Figure 17. (Color online) Impact of Competition on Profits—Faster FDA Approval Reduces NPV of Profits; Longer Exclusivity Increases NPV of Profits



Note. The other two competitors have not entered.

in this industry. Because firms manage a portfolio of products, firm decisions across markets might not be independent. Exploring complementarities across markets is a direction for future work, where one might find that a launched competitor not only affects the market the focal firm is in but also spurs investment in another market belonging to the firm's portfolio. Similarly, there might exist spillovers as firms learn from other firms' successes and failures or from scientific advancements that might encourage R&D over time. Observing investment data alone is insufficient to disentangle these two factors: for example, more entry after the first launch could either be because (1) firms learn this is a profitable market or (2) a scientific advancement makes it easy for the second firm to conduct R&D. Detailed data from the medical literature at the disease level might help control for scientific advancements. I suggest this as an avenue for future research. It was also assumed that, conditional on being in a research state, all firms are equal. Although this assumption seems reasonable given that these firms constitute the top 15 firms in the U.S. pharmaceutical industry, relaxing this assumption and accounting for firm heterogeneity is a direction for future work.

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Appendix. Algorithm to Compute the Equilibrium

This algorithm numerically computes the equilibrium for I firms given the structural parameters θ and FDA approval probabilities pr. The algorithm assumes a finite-time horizon of T years and uses backward induction to find the equilibrium between I firms for each t and each state (x_t, s). In one counterfactual, I set $T = 50$ years, allowing firms to earn profits for 30 years conditional on approval. This setting mimics a world where patent extension is feasible and the time remaining on a drug's patent is not binding, an assumption supported by the findings in Section 2.6 ("Time to patent expiry"). In another counterfactual, I set $T = 20$ years and allow firms to earn profits for 5 years, mimicking a world where patents might be binding and the current market exclusivity period provided by the FDA binds.

1. At the terminal period T, set $v_c(x_t, s) = 0$, $v_f(x_t, s) = 0, v_{ex}(x_t, s) = 0, v_{fFDA}(x_t, s) = 0, v_{exFDA}(x_t, s) = 0$, and $v_l(x_t, s) = u_l(x_t, s)$.

2. At each t, search for a fixed point such that $|f^{l+1} - f^l| < 1e-6$.

3. Given firm value functions at $t+1$, solve by backward induction for the firm value functions at t.

a. Compute the expected future value for every action j that firm i can take in state (x_t, s):

$$EV_j = \sum_{x_{t+1}} \left(\Gamma + \ln \left(\sum_{j'} e^{v(x_{t+1}, s)} \right) \right) \cdot f_j(x_{t+1}|x_t),$$

where

x_{t+1} is a vector of all possible combinations of states that i's competitors can be in;

$f_j(x_{t+1}|x_t) = \prod_{-i} f_{-i}(x_{-i,t+1}|x_t)$ is the probability that the next period's state is x_{t+1}, given that this period's state is x_t and firm i chose action j.

b. Compute the value functions $V(.)$ using Equations (10)–(17).

c. For each firm i, compute the new choice probabilities, f_j^{l+1}, defined by

$$f_j^{l+1} = \sum_{x_{t+1}} \left(\frac{e^{v(x_t, s)}}{\sum_{j'} e^{v(x_t, s)}} \right) \cdot f_j^l(x_{t+1}|x_t).$$

4. Repeat steps 2 and 3 till the condition in step 2 is satisfied.

Endnotes

[1] Firms quote this uncertainty as a disclaimer in their forward-looking press release statements.

[2] Examples include the following quotations: "In recent years, Mr Pharma will complain, the FDA's approval process has become slower" (C.H. 2011), and "FDA approval of new products is deterring new investment in innovation"(quoted in Rappeport (2011)).

[3] Grabowski and Kyle (2007) estimate that market exclusivity periods range from 10 to 15 years, compared with the 20-year patent term awarded.

[4] For example, Hiltzik (2016) called the act "a huge deregulatory giveaway to the pharmaceutical and medical device industry," and the cardiovascular division head at the Cleveland Clinic stated that "the powerful pharmaceutical lobby has helped turn the bill into a gift for drugmakers at the expense of patients" in a statement to NBC News (Fox 2015).

[5] This is similar to a lowering of the entry threshold described in Bresnahan and Reiss (1991b).

[6] See Gilbert (2006) for a review of the theoretical and empirical literature on competition and innovation.

[7] R&D investments that influence existing product quality or existing capacity have been the focus of empirical works such as Gowrisankaran and Town (1997) and Ryan (2012). See Doraszelski and Pakes (2007) for a review of other empirical applications.

[8] This is according to the Pharmaceutical Research and Manufacturers of America. See http://plg-group.com/wp-content/uploads/

2014/03/Pharmaceutical-Profile-2006-Phrma.pdf. Accessed March 2, 2020.

[9] I refer to time spent in research as investment. Firms rarely disclose R&D investments in dollar amounts by disease indication.

[10] To ease the computational burden, I restrict the considered drugs to those affiliated with the top 15 firms by sales. I further consider only the first drug a firm entered a market with (thus potentially ignoring complementarities within a market), which brings down the number of markets from 513 to 294.

[11] See http://www.centerwatch.com/clinical-trials/listings/default.aspx?View=Areas. Accessed August 2017.

[12] To further justify this assumption, I divide the top 15 firms into two groups: those that have invested in many markets versus those that have invested in a few. At the extreme end, Pfizer has clinical trials in nearly 82 markets and Abbott only in 19 markets. This could account for asymmetry in firms. I run a similar regression as in Table 4 but with additional interactions of each of the dependent variables with an indicator for firms that have invested in many disease markets. I do not find any evidence that firms that invest in more markets differ in terms of their responses to various competitor states, which justifies the assumption of symmetric firms. I also check whether company fixed effects (recovered in Table 4) differ significantly from each other in explaining a firm's decision to continue investment, after controlling for all variables and market and time fixed effects. I do not find any significant difference in firm-level fixed effects, indicating these top 15 firms are fairly similar.

[13] For example, the ADIS data set contains the drug name "ethosuximide," launched for "absence seizures" in 1997 with the originator being "Pfizer." Putting in two of these keywords brings up two results in the USPTO database (putting in all three keywords results in no result being found), which were filed in 2014 and 2015 and hence not relevant to the drug launched in 1997. This perhaps implies that Pfizer acquired this drug from another institution (typically a research university). Searching instead for the drug name and indication leads us to 38 possible patents. Going through each of these patents individually reveals that some of the earlier patents are likely to be associated with this drug, but there is no way of knowing which one. Moreover, firms often file more than one patent specific to a molecule/indication: Ouellette (2010) reports that the average patents for drug molecules is 3.5, with the number being higher for drugs with higher sales potential. Collecting such patent data and accommodating it in the model is beyond the scope of the paper, but this could be potentially for future work.

[14] To limit the state space, I assume that once a firm has reached state 5, it continues to remain in state 5 until it exits or files.

[15] These probabilities can be allowed to be a function of the years spent in research prior to filing. This will allow for knowledge accumulation as captured by Doraszelski (2003) and can accommodate, for example, higher approval probabilities if the firm spent more years in research. However, in the data, I do not find evidence supporting this: FDA approval probabilities are almost equal across all levels of investment.

[16] A recent literature uses outcomes from clinical research studies to study the diffusion of pharmaceutical innovations (e.g., Azoulay (2002), Ching and Ishihara (2010), Sood et al. (2014), Ching et al. (2016), and Ching and Lim (2020)). This body manually collects, for a small number of drugs (2–7) (1) journal publications and citation counts (Azoulay 2002), (2) average and standard deviation of the efficacy reported in clinical studies (Sood et al. 2014), or (3) codes the content of each clinical study to a multidimensional attribute space (Ching et al. 2016, Ching and Lim 2020). Doing so for the large number of drugs (over 300) studied in this paper requires automation. Although collecting journal publications and citation counts might be feasible, coding the result of each study requires manually creating an ontology framework so the algorithm can understand the meaning of the text in context, determining in each context which effects are desirable or harmful. Such a task is beyond the scope of this paper and a direction that future research could take.

[17] However, as one gets access to more years of data, and as more drugs launch in the market, more accurate inferences can be made using demand data.

[18] Although each firm can be in 10 possible states, implying a summation over 10^{I-1} possible future states just one period ahead, a simplification occurs because each firm can be in a maximum of three future states. To see this, if a firm is an entrant, it can be in only two possible states next period; if it is an incumbent, it can be in only three possible states next period; and if it has filed, it can be in only three possible future states next period. This results in a smaller state space of maximum dimension 3^{I-1} one period ahead.

[19] In a two-period model, $\pi^1 f(pr_I)$ would be $\pi^1 \times \beta \times pr^I$.

[20] Another source of identification would be if FDA approval probabilities were different under different states (e.g., if a firm filed after three years of research, it was more likely to receive approval). However, such an assumption would lead to unrealistic predictions (i.e., firms would wait until year 3 to file with the FDA). The current model assumes such filing decisions are driven by a stochastic element, which is perhaps closer to reality.

[21] Firms pay a nominal fee to file with the FDA. According to the FDA (2017), this fee was $1.2 million in 2018, a small fraction compared with the amount spent in R&D.

[22] I thank a reviewer for this suggestion.

[23] Such early entry is also consistent with the deterrence literature, where firms enter early to deter future competitors (e.g., Shen and Villas-Boas (2010)).

[24] It is possible that in some markets research costs are skewed negative. For example, in some markets, firms might be encouraged by the government to conduct research in otherwise unprofitable markets. To verify whether this is a possibility, I collect additional data from the National Institutes of Health, U.S. Department of Health and Human Services (National Institutes of Health 2019), to identify which disease markets receive funding (and how much) from the government. I then correlate the estimated classification of market types and the NIH funding by therapeutic area and disease market. I find markets classified as type 2 (in Specification 2) are more likely to receive NIH funding. Type 2 markets include markets such as infections, oncology, immunology, and vaccines, areas which receive disproportionately higher government funding and which might be underresearched if left to firms. We might therefore see firm investment even when market forces deem it unfit for research.

[25] Mestre-Ferrandiz et al. (2012) cite development costs from Phase 1 to Phase 3 at about $215–$220 million. The study also reports that no consistent estimates exist of the magnitude of the cost of the different clinical trial phases. Given that Phase 3 is the longest and costliest part of R&D, I assume a Phase 3 cost of $200 million to quantify the wasteful investment upon exit.

[26] There is no equilibrium computation in the nonstrategic case.

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