Startup Acquisitions and Innovation in the Biopharmaceutical Industry

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Abstract

Big pharma is increasingly using acquisitions to fill their R&D pipelines and the proliferation of the biotechnology industry has created a thick market of innovative target startups. This paper analyzes the dynamic equilibrium effects of biotech startup acquisitions by big pharma on drug innovation and entry. Using a novel dataset on 175 acquired startups from 2000 - 2018, I document several new facts regarding the R&D outcomes of acquired drug projects and entry behavior of startups in markets where acquisitions occur. Motivated by this evidence, I build a dynamic oligopoly model of the pharmaceutical industry featuring big firms and startups that endogenizes drug development, startup acquisitions, product market competition, and entry. Firms select on unobserved project quality at each phase of R&D and into acquisition, allowing higher quality projects to reach later phases of R&D and be a more likely acquisition target. Counterfactual simulations focused on oncology markets suggest that banning startup acquisitions leads to a decline in entry among low-quality startups, who benefit most from lower R&D costs of their acquiring big firms. This and higher selection on quality during R&D among startups results in a decrease in the number of projects that reach the product market and an increase in their quality. Both of these effects are generally small in magnitude. This result directly informs recent discussions among regulators who have expressed concern about the implications of startup acquisitions for market concentration and innovation in the pharmaceutical industry.

JEL Codes: G34, L13, L22, L40, L65, M13, O30

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1 Introduction

Innovation has long been acknowledged as an important driver of economic growth (Aghion & Howitt 1992; Romer 1990). Pharmaceutical innovation in particular has been critical in promoting the longevity and quality of human life. Of the 3.3-year increase in U.S. life expectancy from 1990 to 2015, advancements in pharmaceuticals accounted for 35% or 1.16 years (Buxbaum, Chernew, Fendrick, & Cutler 2020). In recent decades, biotechnology startups have emerged as a significant source of cutting-edge technology and innovative new therapies. Several key technological breakthroughs in pharmaceutical R&D, changes to patent laws and other policies, and increased access to venture capital and private equity funding have led to a proliferation in the number of biotechnology startups.[1] While a few early biotechnology startups such as Genentech, Amgen, and Biogen grew in scale to rival that of big pharma, many startups remained small and focused on drug discovery and early-stage development. As a result, many of the drugs and technologies originally developed by startups are then licensed or acquired by larger firms to carry out late-stage development. By the late 2010s, startups were originating around 70% of the drugs being developed in the U.S.[2] Big pharma, defined here as the top 40 firms by revenue in a given year, has been increasingly using acquisitions as a way to fill their development pipelines. Consequently, acquisition has become an important exit strategy for startups, with around 55% of venture capital-funded biotech startups exiting via shutdown, 24% via acquisition, and 21% via IPO from 2005 through 2015 (Eisfeld 2023).

This paper seeks to understand the dynamic equilibrium effects of startup acquisitions by big pharma, particularly focusing on entry and innovation by startups. To answer this question, the empirical strategy has two steps. First, I construct a novel dataset that enables me to track target startups and their ongoing projects over time by merging comprehensive pharmaceutical R&D data with data on startup acquisitions by big pharma. A project is defined as a drug-disease pair. Using this data, I present descriptive evidence for the relationship between acquisition and the success of acquired startup's projects by comparing the transition probabilities across the phases of pharmaceutical R&D of projects belonging to acquired startups ("acquired" projects) to those of non-acquired startups ("non-acquired" projects). Next, I build a dynamic oligopoly model of the pharmaceutical industry featuring individual unobserved heterogeneity and endogenous pharmaceutical development, startup acquisitions, and entry. Due to the large number of firms in each market, I adopt a moment-based equilibrium concept (Ifrach & Weintraub 2016). The

[1] See Figure 1.
[2] See Figure 3

model is estimated using a nested fixed point algorithm where the objective function is formulated following Arcidiacono, Bayer, Blevins, and Ellickson (2016). I then use the estimated structural parameters of this model to perform counterfactuals that limit startup acquisitions.

The descriptive analysis leads to four key findings: (i) oncology is the most popular therapeutic category for acquired projects at 29% of all acquisitions; (ii) on average, acquired startups have approximately six ongoing projects at the time of acquisition, at most two of which have passed phase I; (iii) acquired projects are 11.6 percentage points (ppt) more likely to successfully complete phase III development than non-acquired projects and 5.39 ppt more likely than big firm projects; (iv) acquired projects in preclinical development, phase I, and phase II are persistently negatively selected with success probabilities lower than both non-acquired and big firm projects at these phases; (iv) an acquisition event in a particular market is associated with a small decrease in entry of fewer than one firm by both startups and all firms in the quarter of and four quarters after an acquisition.

However, the fundamental identification challenge is that acquisition is endogenous. The unobserved quality of the acquired projects is likely correlated with the decision to acquire, creating a selection problem. Using a structural model together with demand data for FDA-approved drugs, we can help disentangle selection from the effect of acquisition on innovation and entry. We build a dynamic oligopoly model of the pharmaceutical industry in continuous time which features endogenous R&D decisions, startup acquisitions, product market competition, entry, and exit. The model features incomplete information via individual unobserved heterogeneity regarding project quality and heterogeneity across firm sizes. Single-project firms begin as potential entrants that take a draw from an initial distribution of project quality, which is fixed over the life of the project, and decide whether to enter R&D. Big firms may alternatively enter R&D through the acquisition of a startup for which they pay a fixed cost that varies with the phase of the target. R&D consists of three phases corresponding to the phases of clinical trials. Firms that choose to enter incur flow R&D costs that vary by phase. At the end of each phase, firms choose to either continue to the next phase of R&D or permanently exit. Projects that receive FDA approval– which is modeled as a random draw taken in exchange for paying a fixed FDA review cost– proceed to the product market where they earn profits. The level of profits a project earns depends upon project quality. The firm earns positive profits until there is generic entry that replaces the project or the project is exogenously discontinued.

The key feature of the model is that firms observe their own project quality when deciding to advance through R&D and potential acquirers observe the project quality of their

target startup. Therefore, selection on project quality across the phases of R&D and into acquisition is endogenous. The implication is that higher-quality projects are more likely to advance to the product market and are more likely to be acquired. Project quality is unobserved to the econometrician. To produce a measure of project quality, I merge revenue and quantity data for approved projects into the existing dataset. Project-level profits are estimated according to a reduced form that is a function of the state variables. Project quality maps directly into the project fixed effect in the profit equation, defining it as the mean monopoly profits of the project. The initial distribution of project quality can then be backed out using the quality estimates for projects that reach the product market together with the selection mechanism provided by the model that determines the transition rate across the phases of R&D.

Due to the presence of several competing mechanisms, the effect of acquisitions on innovation and entry by startups are not clear ex-ante. In regards to innovation, the presence of economies of scope or scale in R&D would increase the probability of success among acquired projects by bringing them into a firm with a larger scale and broader scope (Cockburn & Henderson 2001; Danzon, Nicholson, & Sousa Pereira 2005; Henderson & Cockburn 1996). Access to greater financial resources and synergies between R&D programs may also increase the probability of success. On the other hand, there may be diseconomies of scale, as big firms may hinder innovation through bureaucracy and the distortion of acquired researchers' incentives relative to small, closely held startups (Cockburn 2004). Big firms may also be engaging in killer acquisitions intended to shut down the projects of the target firm that will potentially compete with those of the acquirer. Cunningham, Ederer, and Ma (2021) find that about 5-7% of acquisitions in the pharmaceutical industry are "killer acquisitions". As a result, the equilibrium effect of acquisition on innovation outcomes for acquired projects is theoretically ambiguous. In regards to entry, lucrative acquisition markets provide a profitable exit strategy for startups and will therefore promote entry (Phillips & Zhdanov 2013). On the other hand, entry of big firms via acquisition can reduce follow-on entry by startups due to increased competition (Eisfeld 2023). Firms may be dissuaded from entering as the proportion of big firms competing in the market increases. This effect is not limited to startups and may also affect innovation by incumbent firms by reducing their transition probabilities.

I investigate these mechanisms empirically in the descriptive analysis and use the results to motivate the assumptions made in the structural model. I find that big firms are more likely to advance at each stage of R&D except phase I, suggesting that some agglomeration of economies of scope and/or scale, access to financial resources, or lower opportunity costs outweigh potential diseconomies of scale. This finding is incorporated into the

model by allowing the flow costs of R&D to vary by firm size. I also find no statistically significant evidence for killer acquisitions in my data, which is a particular subset of the dataset constructed in Cunningham et al. (2021). As a result, I abstract away from multi-product firms and model firms as having one singular project. I find a small statistically significant negative effect of acquisition on entry immediately following the acquisition. This is incorporated into the model by allowing acquisitions to change the ratio of startups to big firms, which changes the focal firm's perceived transition probabilities of competitors. I also allow for the opportunity for acquisitions to increase entry among startups, an effect that cannot be investigated empirically. To simplify the structural model, I do not include a preclinical phase and firms instead enter directly into phase I. However, the transition rate from preclinical to phase I is incorporated into the model through the entry rate. Lastly, I find that competition affects innovation efforts by all firms. Firms are less likely to advance to the next phase of R&D as their log number of competitors increases, particularly those in the same or higher phases. In the model, firms keep track of the number of competitors in each phase of development and the profit function depends negatively upon the number of approved projects.

The estimated model fits the data reasonably well, matching most of the targeted transition rates within 5 ppt, replicating the shape of the quality density for approved projects with a large degree of overlap, and predicting market-level phase-specific acquisition counts that are consistently within the 95% confidence intervals implied by the data. The model performs the weakest on the transition rates for acquired projects in non-oncology markets, where the transition rates are consistently over- or under-predicted by more than 5 ppt. The estimated quality density for approved projects in the data suggests that over 85% of approved projects make monopoly profits of less than $25 million per quarter in year 2005 dollars. The remaining 15% belong to a long right tail reaching up to $1 billion per quarter. This is consistent with blockbuster drugs being a salient feature of the pharmaceutical industry. The estimated initial quality distribution from the model suggests that the mean project drawn at the beginning of R&D makes monopoly profits of more than $1.1 million per quarter, which is consistent with the high attrition rate in pharmaceutical R&D. The total costs of development are large at approximately $412 million for startups and $303 million for big firms in non-oncology markets and $563 million and $177 million in oncology markets. The difference in total costs results from lower flow costs in phases I, III, and FDA review for big firms. Finally, the fixed costs of acquisition are increasing in the phase of the acquired startup with the fixed cost of acquiring a phase III firm at $131 million.

In the main counterfactual of this paper, I consider a ban on startup acquisitions. This

is operationalized by setting the arrival rate of opportunities for big firms to acquire equal to zero. The results are currently focused on oncology markets, where the model-implied transition probabilities for acquired projects fit the data well. A comparison of data simulated from the estimated and counterfactual models reveals that such a ban will have several effects on oncology markets in equilibrium. First, there is a decline in the startup entry probability of 6.5 ppt driven by low- and mid-quality startups. Acquisition disproportionately benefits these firms because they are likely to be among the marginal firms deciding whether to advance to the next consecutive phase when faced with the higher R&D costs of startups. Second, low- and mid-quality startup projects that reach phase III and would have otherwise been acquired now face higher FDA review costs as startups. High-quality projects, on the other hand, are likely to reach marketing regardless of which firm type owns them. This results in fewer projects reaching marketing across all market sizes, though the reduction in the number of approved projects in fairly small. The largest declines occur in medium-sized oncology markets where the number of approved projects decreases by 1.1 projects (21.2%). Conditional on reaching marketing, the density of high-quality projects increases relative to low- and mid-quality projects. The change in the mean quality is equivalent to a change in the mean monopoly profit in a large market from $109.68 to $135.97 million per quarter or a 23.97% increase in mean profit.

The interaction between innovation and acquisition in the pharmaceutical industry is the subject of ongoing policy debate. In March 2021, the Federal Trade Commission (FTC) and regulatory authorities from Canada, the U.K., and the E.U. announced they would create a multilateral working group tasked with building a new approach to evaluating pharmaceutical M&A.[3] Among the objectives of the group was to evaluate the "full range of a pharmaceutical merger's effects on innovation". In June 2022, the working group held a two-day public workshop attended by regulatory officials and a variety of academics, health policy, and antitrust experts. Panelists expressed concern regarding acquisitions of nascent competitors which often fall below the HSR pre-merger notification threshold and its implications for market concentration and innovation.[4] This study directly informs this policy discussion by providing empirical estimates of the equilibrium effects of startup acquisitions on innovation as measured by the transition probabilities of acquired projects through R&D and on subsequent entry of new projects by startups.

The remained of the paper is organized as follows. Section 2 reviews related literature and the contribution of this paper. Section 3 discusses the relevant institutional features

[3]See https://www.ftc.gov/news-events/news/press-releases/2021/05/multilateral-pharmaceutical-merger-task-force-seeks-public-input

[4]For transcripts of workshop proceedings, see https://www.ftc.gov/news-events/events/2022/06/future-pharmaceuticals-examining-analysis-pharmaceutical-mergers

of the biopharmaceutical industry. Section 4 introduces the data sources and the sample construction methodology. Section 5 presents descriptive evidence that will motivate both the model and the results. Section 6 describes the model while Section 7 describes its identification and estimation. Section 8 presents the parameter estimates and the results of the counterfactual. Section 9 concludes.

2 Related Literature

This paper studies the relationship between innovation, acquisitions, and competition, and primarily contributes to three strands of literature studying the bilateral relationships between each of these topics.

There is no theoretical consensus on the precise relationship between competition and innovation. The "escape competition" effect suggests that an increase in competition will increase R&D investment as firms compete for innovation rents, while the Schumpeterian effect suggests that firms will reduce R&D investment due to the risk of obsolescence (Aghion, Bloom, Blundell, Griffith, & Howitt 2005). In the industrial organization literature, different studies have reached different conclusions regarding the relationship between innovation and competition depending on the context (Goettler & Gordon 2011; Hollenbeck 2020; Igami & Uetake 2019). Which effect dominates likely depends on the level of competition and industry-specific institutional details. Focusing on the pharmaceutical context of the current study, Rao (2020) finds that competition has a negative impact on investment in pharma using data on development decisions from phase III clinical trials. However, using an equilibrium model of dynamic R&D investment, they find that policies aimed at increasing the length of exclusivity and reducing FDA approval time encourage investment despite the increase in competitive intensity. Khmelnitskaya (2023) extends this study to incorporate all phases of clinical development and separately account for attrition due to competition versus attrition due to scientific failure. They find that 8.4% of all attrition is strategic though this is highly heterogeneous across markets, suggesting that differentiating between attrition due to competition and attrition due to science is important for correctly interpreting policy implications aimed at increasing innovation. The present study will build on the preceding two using a continuous time model of drug development with competition. Importantly, I will diverge by incorporating individual unobserved heterogeneity at the project level, which is going to capture dynamic selection across the phases of R&D and selection into acquisition. Doing so will disentangle attrition due to competition from attrition due to vertical quality differences.

A related (and often overlapping) literature explores the relationship between M&A

and competition. Many papers in industrial organization have studied M&A using static models to understand the counterfactual impact of a merger on prices and market structure (see Nevo 2000). The first paper to examine M&A in a dynamic setting was Gowrisankaran (1999), which created a computational model capable of fully endogenizing the choice to merge and allowing players to be forward-looking when proposing mergers. This endogenous mergers framework has been applied to various industries in a handful of papers (Hollenbeck 2020; Igami & Uetake 2019; Jeziorski 2014). In the paper most closely related to the present paper, Eisfeld (2023) examines the impact of exogenous startup acquisitions on entry decisions by startups in a dynamic model of the software industry. They find that while startup acquisitions overall provide an entry-for-buyout incentive that increases entry, startup acquisitions by large firms that were previously absent from the market discourage follow-on entry through the change in market structure. In contrast to this paper, I will endogenize the startup acquisition decision by explicitly modeling a one-shot acquisition decision by big firms and by allowing them to interact with startups in equilibrium. I will also be able to analyze the effect of startup acquisition on innovation as well as entry decisions using data on the R&D outcomes of acquired projects.

Lastly, this paper contributes to the (mostly reduced-form) literature that examines the relationship between M&A and innovation, particularly as it relates to the pharmaceutical industry. Focusing on how innovation affects M&A decisions, both Higgins and Rodriguez (2006) and Danzon, Epstein, and Nicholson (2007) find that M&A in the pharmaceutical industry is motivated by declining internal productivity and that firms use acquisitions to fill gaps in their R&D pipelines. Empirical evidence for the reverse effect of M&A on innovation is scarce. Aggarwal and Hsu (2014) analyze the impact of going public or being acquired on firm-level innovation among biotechnology firms as measured by patent counts and forward citations. The authors find that patent counts increase relative to both private and public firms but patent citations decrease. The authors conclude that staying private generates the best innovation outcomes, followed by acquisition, then going public, suggesting that information disclosure is an important mechanism affecting patenting. Cunningham et al. (2021) highlight one particular incentive for M&A in the pharmaceutical industry, which they call the "killer acquisition" motive. They find that 5–7% of M&A in the pharmaceutical industry are killer acquisitions, where firms acquire targets developing projects in overlapping therapeutic areas in order to shut the project down and preempt competition in downstream product markets. In this paper, I will estimate the dynamic equilibrium effect of startup acquisitions on innovation by considering a number of mechanisms through which acquisitions can affect innovation including killer

acquisitions.[5]

3 Institutional Details

3.1 Pharmaceutical R&D

In the U.S., the Food and Drug Administration (FDA) is responsible for ensuring the safety and efficacy of marketed drugs and firms must follow the regulatory procedures set out by the FDA when seeking to develop a new drug. The first stage of the pharmaceutical R&D process is discovery and target identification. In this stage, firms and scientists identify potential drug targets, which are specific molecules or biological processes involved in a disease. This stage often utilizes high-throughput screening techniques and computational models to identify and test thousands of compounds with the potential to interact with the target. Compounds that act on the target in a way that helps to treat the disease of interest may become a drug candidate. Once a drug candidate has been identified, the drug enters the preclinical testing stage. In this stage, potential drug candidates undergo rigorous laboratory testing and animal studies to assess their safety, efficacy, and potential side effects. Preclinical testing helps researchers understand how the drug works, its dosage, toxicity levels, and potential interactions. If preclinical testing shows promising results, the firm must file an Investigational New Drug (IND) Application with the FDA before clinical research in humans may begin. The IND contains the data gathered during preclinical research and the proposed clinical trial protocols. If the FDA finds IND acceptable, then it may proceed to clinical trials.

Clinical trials are typically conducted in three phases to gather data on the drug's safety and effectiveness in humans. Phase I trials are typically several months to one year in length and include a small group of healthy volunteers who will be randomly given the drug in various doses to test its safety and appropriate dosing. Phase II trials typically last several months to several years and expand the study to test the drug on up to several hundred volunteers within the target patient population in order to test the drug for both safety and efficacy for its intended use. Phase III trials typically take several years to complete and involve several hundred to several thousand volunteers within the target patient population to gather extensive data on safety, efficacy, and side effects in comparison to existing treatments. If the clinical trial data demonstrate that the drug is safe and effective, the pharmaceutical company submits a New Drug Application (NDA) or a Bi-

[5]The competing effects of horizontal mergers on innovation, both helpful and harmful, are well summarized in Federico, Morton, and Shapiro (2020).

ologic License Application (BLA) to the FDA depending on the type of drug. The NDA (BLA) includes comprehensive data on the drug's safety, efficacy, manufacturing details, and proposed labeling. A team of FDA scientists, including physicians, statisticians, and other experts, conducts a thorough assessment of the NDA (BLA). If the FDA determines that the drug's benefits outweigh its risks and the firm has provided sufficient evidence, it grants approval for marketing the drug. After approval, the FDA monitors the drug's safety and effectiveness through post-marketing surveillance. Adverse events and side effects are reported to the FDA, and the agency takes appropriate regulatory actions including relabeling or discontinuation of the drug, if necessary.

Pharmaceutical R&D is inherently risky financially due to the high costs of preclinical and clinical development and the high attrition rate of compounds at each stage of R&D. According to the FDA, approximately 70% of drugs that enter phase I transition to phase II, 33% transition from phase II to phase III, and 30% transition from phase III to regulatory review. Each consecutive phase of clinical trials grows both in duration and in the number of participants, which causes them to also grow in costs. DiMasi, Grabowski, and Hansen (2016) estimate the mean time to the next phase (phase length) of phase I, II, and III to be approximately 1.65 (2.75), 2.53 (3.16), and 2.55 (3.76) years, respectively. Among drugs that were eventually tested in humans, the mean time from synthesis to initial human testing was 2.60 years. Regulatory review had a mean duration of 1.33 years. The mean time to next phase and the phase length may differ from each other and from the typical phase lengths described in the preceding paragraphs for a couple reasons. First, they are inclusive of the waiting times between finishing a clinical phase and advancing to the next phase. During this time, firms will be analyzing the data collected during the trial and weighing pipeline management decisions. Second, firms will also conduct multiple trials within the same clinical phase for the same drug as they vary the location, design, or disease of interest for each trial. The authors estimate the mean phase costs to be $49.6, $95.3, and $314.0 million in 2013 dollars, respectively, after accounting for the time cost of money. After accounting for the cost of failed drugs, a single approved drug costs $1.36 billion out-of-pocket to take from preclinical research through approval. After accounting for the time cost of money, this figure increases to $2.56 billion.

3.2 Biopharmaceutical Industry

The structure of the biopharmaceutical industry – the umbrella term for both pharmaceutical and biotechnology firms engaged in drug R&D – has changed significantly over the

past 40 to 50 years.[6] Prior to the 1980s, drug R&D in the U.S. was typically carried out by approximately forty large, vertically integrated pharmaceutical firms, or "big pharma". They segued internally discovered drug candidates through the R&D process from discovery to approval and also engaged in marketing, manufacturing, and distribution. Drug candidates at this time were entirely small molecule drugs – drugs that can be synthesized through chemical processes and have a defined chemical structure. As a result, the manufacturing process is generally well-established and can be reproduced consistently. This changed with the development of recombinant DNA technology in the 1970s which enabled scientists to manipulate genes and produce valuable proteins. This breakthrough laid the foundation for the rise of biotechnology and its integration into the pharmaceutical industry in the 1980s. Biotechnology companies pioneered the use of genetic engineering and recombinant DNA technology to develop therapeutic proteins and other biologics. Biologic drugs are large, complex molecules derived from living organisms, such as proteins, peptides, antibodies, or nucleic acids (DNA or RNA). They have a more intricate and diverse structure compared to small molecule drugs. The manufacturing process for biologics requires biotechnology processes involving living cells or organisms, making replication more difficult. While several biotechnology firms including Genentech, Amgen, and Biogen came to be fully vertically integrated and joined big pharma, many remained relatively small, closely aligned with the academic institutions from which their researchers came, and focused on drug discovery and early-stage development.

The development of high throughput screening (HTS) – a method that allows for the rapid screening of large numbers of compounds to identify those that have a potential therapeutic effect, changes to patent laws, and policy changes including the Bayh-Dole Act helped lead to a proliferation in the number of small biotechnology firms in the 1980s and 1990s. HTS led to a significant increase in the number of compounds that can be screened, as well as the speed at which they can be analyzed. This has helped small biotechnology startups to rapidly identify promising drug candidates, reducing the time and costs involved in drug discovery. The ability to patent a wide range of inventions in biotechnology including DNA sequences, proteins, genetic engineering techniques, pharmaceuticals, and diagnostic methods and tools made this industry attractive for profit-driven entrepreneurs. The Bayh-Dole Act further allowed nonprofit research institutions and small businesses to own, patent, and commercialize inventions developed under federally funded research programs within their organizations. The potential for large profits in this industry also attracted venture capital investors who funded many of these startups. As a result, a vertical structure came to dominate the industry. Biotechnology firms engaged

[6]For a more detailed history, see Cockburn (2004).

in drug discovery and proved the viability of a drug candidate in preclinical research and early-stage clinical development. Promising drug candidates may then be licensed out to or acquired by a downstream big pharma firm that can continue its development in the larger, more capital-intensive phases of R&D.

Further proliferation in the biotechnology industry occurred throughout the 2000s and 2010s. As the global population grows and ages, the demand for new and innovative therapies to treat diseases and medical conditions has increased. Small biotechnology startups are well-positioned to develop these therapies, as they are often more agile and focused on specific areas of research. Further scientific discoveries including the development of next-generation sequencing technologies, which allow researchers to sequence large amounts of DNA and RNA more quickly and at a lower cost than traditional sequencing methods, and advances in gene editing technologies such as CRISPR/Cas9 have revolutionized the field of genetic engineering and made it possible to more precisely manipulate and edit the genome of cells and organisms, leading to the development of new therapeutic modalities. Entry by startups into the biotechnology industry can be seen in Figure 1, which shows the count of new startups entering R&D from 1995 to 2017. The number of entering startups in a given year more than doubled over this period, peaking in 2009 with nearly 500 new startups. The data indicate that indeed many of these startups are engaged in drug discovery. Figure 2 shows the count of drugs originated by the 40 largest pharmaceutical firms and by startups by year. From 1995 to 2017, startups have played an increasingly important role in drug discovery, reaching a peak of nearly 1500 drugs originated in 2009. Simultaneously, big pharma has decreased the number of internally originated drugs. This translates to a steep change in the share of drugs in development originated by startups, as shown in Figure 3. By 2017, nearly 80% of all new drugs were originated by startups.

4 Data Sources and Sample

4.1 Firm Size Definitions

A precise definition for *big pharma* firms is created using data from Compustat Global spanning the period from 1990 to 2018. Compustat Global offers comprehensive financial and market data for publicly traded companies across more than 80 countries, encompassing over 90% of the world's market capitalization. From this dataset, I extract annual revenue data for companies categorized under the pharmaceutical, allied chemical, surgical, medical, or dental instruments, or ophthalmic goods industries, which correspond

to Standard Industry Classification (SIC) codes 2800, 2833 - 2836, 3841 - 3845, 3851, and 8731. I rank these firms based on their annual revenue in descending order in each year. Next, I manually exclude large chemical and medical device manufacturers, as well as any other firms that primarily generate revenue from sources other than the development and manufacturing of pharmaceuticals. For a firm to be classified as part of big pharma, it must rank within the top 40 firms on this list for a given year.

The definition used for a biotech startup in the remainder of this paper differs from that described in Subsection 3.2. Biotech *startup* firms are defined as those with no approved drugs or significant alternative revenue streams. Many of these small firms are engaged in biotechnology R&D, although it is not a requirement. To ensure a firm has no previously approved drugs, I gather drug approval data from regulatory authorities in the U.S., E.U., Canada, France, Germany, Australia, Korea, and Japan, covering the years 1900 to 2018. In order to identify potential large alternative revenue streams unrelated to product sales (potentially from contract research or out-licensing), I merge in data from Compustat Global and drop all publicly traded companies with annual revenues exceeding $25 million in year 2000 dollars. A firm is no longer considered a startup once it surpasses the $25 million threshold or obtains an approved drug, whether through licensing or regulatory approval. Additionally, I manually remove any remaining large manufacturers of generic drugs, chemicals, and medical devices that are not included in Compustat. Not-for-profit organizations, governmental entities, and educational institutions are also excluded. Finally, I exclude firms operating as a subsidiary or unit of a non-startup.

Firms that do not meet the criteria for being classified as startups or big pharma will be categorized as *medium* size firms. This category includes firms that do not rank among the top 40 in terms of industry revenues for a given year but who have an approved drug or large alternative revenue stream. These firms will be excluded from the analysis. I continue to exclude not-for-profit organizations, governmental entities, and educational institutions, as their primary objective may not be profit maximization.

4.2 Drug Development Data

I construct a novel dataset that links acquisitions, drug development, and product market competition. The purpose of this dataset is to identify acquired firms and their ongoing projects. Drug development data is accessed through Clarivate Analytics' Cortellis Investigational Drugs database, which covers the time period from 1990 to 2018. Cortellis employs a combination of automated data collection and expert curators to compile comprehensive data on drug candidates from a variety of sources. These sources include

company announcements, press releases, financial reports, clinical trial registries, scientific literature and patents, industry conferences, and regulatory filings. The data is structured as a panel that tracks drug candidates globally over time. Each observation includes the drug's name, the name of the sponsoring firm, the indication or disease under investigation, the current stage of development, the start date of the current stage, the country where the stage is being conducted, the drug's target-based action, the technologies utilized by the drug, any termination decisions, and a brief overview of the drug's development for a given drug-firm-country-indication.

To facilitate analysis, the development stages are categorized into seven bins: drug discovery and preclinical trials, phase I, phase II, phase III, regulatory review, regulatory approval and marketing, and discontinuation. The discovery/preclinical phase will also be referred to as "phase 0". Each indication is mapped into a single three-digit ICD-9 code. The International Classification of Diseases, 9th Revision (ICD-9), developed by the World Health Organization, is a widely used diagnostic coding system that provides a standardized framework for classifying and categorizing diseases, injuries, and other health conditions. There is no consistent or standardized method for listing a drug's intended indication in Cortellis. As a result, drugs intended to treat the same disease or condition may have different indications. Mapping each indication into an ICD-9 allows for the grouping of highly similar indications into markets. For example, the indications "Lung Cancer", "Small-Cell Lung Cancer", "Non-Small-Cell Lung Cancer", "Metastatic Non-Small-Cell Lung Cancer", and "Respiratory Tract Tumor" are all assigned to the ICD-9 code 162, which corresponds to "Malignant neoplasm of trachea, bronchus, and lung".

The level of observation in the final sample is a drug-ICD-9 pair, which I will refer to as a "project". This level of observation aggregates over the sponsoring firms and countries involved in the development of each drug-ICD-9 pair. Consequently, this analysis abstracts from licensing agreements and strategic alliances between firms. To be included in the final sample, I require that at least one clinical trial for the drug be conducted in the U.S., Canada, Australia, or Western Europe.[7] For the regulatory review and marketing phases, I consider only New Drug Applications submitted to and/or approved by the FDA. These criteria limit the sample to drugs that are intended for sale in U.S. markets.[8] This is necessary as I only have drug sales data for the U.S. However, the U.S. is by far the

[7]Western Europe includes Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom, "Europe", and the "EU".

[8]A 2010 study by the U.S. Department of Health & Human Services found that 80% of NDAs approved by the FDA in 2008 contained at least one foreign clinical trial while 8% had exclusively foreign data. Western Europe accounted for nearly 60% of foreign clinical trial sites. See https://oig.hhs.gov/oei/reports/oei-01-08-00510.pdf.

world's largest drug market, accounting for 49% of the pharmaceutical industry's global revenue in 2020 followed by Europe at 23%.[9] Thus, focusing on the U.S. market provides valuable insights into a significant portion of the pharmaceutical industry's revenue and market dynamics. I drop biosimilars and diagnostic agents from the sample. I also exclude ICD-9 239, which includes all projects whose indication is given as "solid tumor" or "cancer".[10] Finally, small markets with a maximum number of competitors less than 16 or fewer than 18 entrants over the course of the sample are excluded.

In addition to the drug development data, Cortellis provides information regarding companies in the pharmaceutical industry, allowing for a linkage between each drug and the characteristics of its sponsoring firm. The company data includes each company's address, ownership status, sector classified as public or private, funding sources including venture capital and private equity, and size classification, which is categorized in ascending order as micro, small, medium, large, or mega. I use the sector and size classification provided by Cortellis as a source of external validation for the firm size definitions in the subsection 4.1.

The coverage of Cortellis improves over time due to several policy in the 1990s and 2000s which increased the public disclosure requirements regarding clinical trials. First, in 1997, the FDA Modernization Act was passed and required the Department of Health and Human Services to establish ClinicalTrials.gov, a registry of clinical trials conducted under INDs. Then, in late 2004, the International Committee of Medical Journal Editors announced that beginning in July 2005 its member journals would require registration in a public clinical trials database as a condition for publication. The FDA further required that beginning in September 2007, any trial conducted in the U.S. or under an IND must be registered with ClinicalTrials.gov. As a result of these changes, I limit the sample to begin in 2000.

Ideally, we would see each project advance through each consecutive phase of R&D until it is discontinued or approved and have a starting date for each phase. However, the data may omit phases or the dates associated with those phases. For example, for a given project, we may observe phase I and its start date, not observe phase II or its start date, then observe phase III and its start date. In these cases, I impute that the project successfully passed all phases preceding the lowest observed phase and all phases between the lowest and highest observed phases. The start dates for these phases are imputed using the start dates for the observed phases and the average phase lengths in the sample. There is also

[9] Source: IQVIA MIDAS database

[10] This ICD-9 is much larger than all others as many early phase (often preclinical) projects are given these general indications. However, there are no approved projects in this ICD-9 precisely because these indications are too general.

a problem of "zombie" projects, or projects that are never officially discontinued. In this case, I manually insert discontinuation observations if eight years have elapsed since the beginning of the phase.

4.3 Acquisition Data

Acquisition data is sourced from SDC Platinum for the period from 1989 to 2018. SDC Platinum is a comprehensive financial database with an extensive collection of global financial data, including data on mergers and acquisitions (M&A), initial public offerings (IPOs), venture capital, and private equity. SDC Platinum's M&A dataset contains information on over 1.3 million global transactions dating back to the 1970s. Detailed information about each transaction is provided including the acquiring and target company, their respective parent companies, deal value in nominal dollars if available, deal structure, announcement and effective dates, the acquiring firm's stake in the target pre- and post-acquisition, and a brief description of the transaction. To be considered an acquisition in the final sample, the acquirer's ownership stake must meet certain criteria. Specifically, the acquirer must hold less than or equal to 50% of the target company pre-transaction and greater than 50% of the target company post-transaction. Further, the acquirer or the acquirer's parent company must appear on the list of big pharma firms defined in subsection 4.1 in the year of the acquisition. At this point, the sample includes all acquisitions made by big pharma firms. To identify acquisitions of startups, the names of target firms in this sample are matched to the names of startup firms identified in Cortellis, which I detail further in subsection 4.5.

4.4 Drug Demand Data

Drug sales data is collected from the IQVIA MIDAS database and covers the period from the second quarter of 1997 to the first quarter of 2011. This database provides quarterly wholesale volume (quantity) sales and revenue data for all drugs, both branded and generic, sold by each firm in the United States. The revenue data is adjusted to a base year of 2005 using the CPI. The volume data is measured in terms of standard units (SUs), which allows us to aggregate volume sales across different dosage forms for the same drug. IQVIA defines a standard unit as "the smallest common dose of a product form", such as one tablet or capsule for solids, 5 ml for liquids, and one ampule or vial for injectibles. Quarterly prices are determined by dividing revenue by sales volume.

IQVIA MIDAS also provides quarterly-level data on product-specific advertising spending. This includes direct-to-consumer (DTC) advertising, which comprises all U.S. televi-

sion, radio, and print ads targeted at the general public for a particular drug. Pharmaceutical firms also engage in advertising aimed at healthcare professionals, such as medical journal advertising, direct mail campaigns, and interactions between pharmaceutical sales representatives and physicians (referred to as detailing). The spending data included in this analysis will be the summation of these various forms of advertising.

To estimate the quarterly potential market size for each ICD-9 code, ideally, we could measure the total willingness to pay of society to eradicate the diseases associated with that ICD-9. For a subset of the ICD-9s in Cortellis, this can be achieved by utilizing epidemiological data from the Global Burden of Disease (GBD) provided by the Institute for Health Metrics and Evaluation at the University of Washington. The GBD aims to provide a comprehensive understanding of the global burden of diseases, injuries, and risk factors by integrating data from various sources such as vital registration systems, surveys, censuses, and scientific literature. Specifically, I extract disability-adjusted life years (DALYs) data for a range of diseases in the United States from 1990 to 2018. DALYs equal the sum of years of life lost and years lived with disability, both of which are affected by prevalence, incidence, mortality, and disease duration. DALYs can be converted into a willingness to pay using the value of a statistical life-year (VSLY). Having obtained an estimate of the potential market size for each disease, we can then utilize the disease to ICD-9 crosswalk provided by the GBD database to estimate the total willingness to pay for each ICD-9 code.

However, this data is only available for a subset of the ICD-9s. Instead, I use the number of entrants into the preclinical phase for the entire sample period as a proxy measure of potential market size that is available for every ICD-9 in the data. I use this measure assuming that the number of entrants into preclinical is correlated with potential market size, an assumption that is supported empirically. The correlation between the willingness to pay estimate and the number of entrants for the subset of ICD-9s for which the willingness to pay is available is 0.45. In the structural analysis that follows, potential market sizes will be grouped into three categories: small, medium, and large. Section 7.2.4 provides precise definitions of each category.

4.5 Final Data Sample

The process of combining the final SDC and Cortellis samples begins with standardizing the sponsoring firm names in Cortellis and the target names in SDC. This standardization involves removing company suffixes and punctuation, as well as standardizing common terms within each name. A fuzzy merge of the two datasets is performed using the standardized firm names and addresses to identify the acquired startups. The accuracy of each

match is manually verified. One complication of the matching process is that many drugs are licensed between firms, so the sponsoring firm's name for each project may change over time. To deal with this, I assign ownership of each project to the originator firm for the entire project duration, so long as the project is not in the sample of acquired projects. For projects originated by universities or not-for-profits, I assign the first licensed firm on the project as the originator. Therefore, acquired projects will be projects that were originated by the startup.[11] Only acquired projects will experience a change in the size of the firm developing them.

When a big pharma firm acquires a startup, it acquires all of the startup's active projects. The startup's active projects at the time of acquisition are referred to as *acquired* projects. Specifically, an acquired project spans the startup's acquisition date with development events observed both before and after acquisition. This includes cases where the only event post-acquisition is project discontinuation. I also include projects that began entirely after the acquisition as acquired if another project for the same drug (but a different ICD-9) was acquired by the previous definition. Therefore, a *non-acquired* project is a project conducted by a startup that was not acquired for the entire duration of the project nor any other projects for the same drug.

The resulting dataset is merged with the drug demand data from IQVIA based on drug name.[12] IQVIA reports revenues at the drug level. To get revenue at the project level, I assume that drug revenue in a particular quarter is split evenly among each approved project for that drug in that quarter.

5 Descriptive Evidence

5.1 Summary Statistics

The final sample spans the years 2000 to 2018 and contains 1,096 acquired projects, corresponding to 175 acquired startups with 592 drugs. Figure 4 shows the count of acquired startups by year. From 2000 to 2004, the average number of acquisitions per year is less than five. After this period, the number of yearly acquisitions jumps and averages around twelve per year from 2005 to 2018. This trend is at least partially due to the improvements in Cortellis's coverage discussed in subsection 4.2, as we are only counting the acquired startups corresponding to the acquired projects we can identify. Figure 5 shows the distribution of acquired projects across therapeutic categories. Therapeutic categories are based

[11] 74% of acquired startups' active projects at the time of acquisition were originated in-house. Therefore, most startups are being acquired for projects that originated in-house, not ones that were in-licensed.

[12] 95% of approved drugs in the final sample are successfully matched to drugs in the IQVIA dataset.

on commonly defined therapeutic categories for pipeline drugs used among big pharma firms including infectious diseases, oncology, metabolic and endocrine disorders, cardiovascular diseases, neuroscience, respiratory diseases, immunology, and other.[13] The oncology category contains approximately 28.7% of acquired projects and is by far the most popular category for acquired projects. In addition to the large size of the oncology market, a given oncology drug is often tested for many ICD-9s within the oncology category, resulting in many oncology projects.

We can also look at the distribution of acquired projects according to their phase. The left-hand y-axis of Figure 6 provides the count of acquired projects across phases at the time of acquisition. Approximately 56% of acquired projects are in the discovery and preclinical phase. Most of the remaining projects are in phase I or II. Only around 6% of acquired projects are in phase III or undergoing FDA review. If we divide the total count of projects in each phase by the number of startups acquired, we can get an idea of what the "average portfolio" of an acquired startup looks like. This is on the right-hand y-axis of Figure 6. The average acquired startup has 6.2 projects. Approximately 3.5 of these projects are in discovery/preclinical, 1.1 projects are in phase I, 1.3 projects are in phase II, and 0.3 projects are in phase III or FDA review. There is, however, some heterogeneity in the portfolio of acquired firms. Figure 7 gives the distribution of acquired firms according to their highest phase project. As we would expect from the average portfolio, the majority of acquired startups have at least one project in phases II, III, or in FDA review. Surprisingly, around 32% of acquired firms only have projects in discovery/preclinical or phase I.

Summary statistics for startups' projects by acquisition status are given in Table 1. The first five rows of this table are the conditional transition probabilities across phases. That is, *ReachPhasek+1* measures the probability that a project advances to phase $k+1$ conditional on being in phase k. Among all startup projects, 36.6% transition from preclinical to phase I, 78.0% from phase I to phase II, 33.0% from phase II to phase III, 44.7% from phase III to FDA review, and 84.2% from FDA review to approval. This implies that around 3.6% of startup projects that ever enter preclinical development are eventually approved.[14] We can compare the transition probabilities across acquisition status. Acquired projects are 2.3 ppt less likely to advance to phase I, 13.2 ppt less likely to advance to phase II, 3.4 ppt

[13]ICD-9s are assigned to therapeutic categories using the following mapping: oncology (140-239), neuroscience (290-359), immunology (279, 555-558, 691, 695-696, 710-716, 720), infectious disease (1-139), cardiovascular (280-289, 390-459), respiratory (460-519), endocrinology/metabolic (240-278), other (260-289, 520-553, 560-690, 692-694, 697-709, 717-719, 721-999).

[14]These transition probabilities are very similar to the transition probabilities provided by the FDA cited in subsection 3.1 with the exception of the phase III transition which is considerably higher.

less likely to advance to phase III, 13.9 ppt more likely to advance to FDA review, and 8.1 ppt are likely to gain FDA approval. We will investigate these transition probabilities more rigorously using regression analysis with various controls. We can also compare the transition probabilities across firm sizes using Table 2, which provides the summary statistics for projects by firm size. Across all phases except I, big firms are more likely to reach the next consecutive phase. Big firms are 17.4, 4.8, 8.6, and 4.2 ppt more likely to reach phases I, III, FDA review, and marketing, respectively. They are 4.1 ppt less likely to reach phase II.

The next group of variables in each table, *CompPhasek*, measure the number of competing projects in phase k in the same ICD-9 at the time of the focal project's transition from a given phase. From Table 2, we can see that the median market across all firms' projects has approximately 127.3 projects in R&D at any given time, though the standard deviation indicates there is significant heterogeneity in the size of the market. The vast majority of these projects are in the preclinical phase with a high attrition rate between preclinical and in-human trials. Big firms and startups on average tend to compete in markets with similar distributions of the number of competitors. Acquired startup projects belong to markets with a larger number of competitors in the clinical phases of development.

The third group of variables shows that, on average, acquired projects are less likely to be biologics with 40.0% of non-acquired projects having a *Biologic* indicator equal to one compared to only 34.9% of acquired projects. Projects being developed by big firms are nearly 20 ppt. less likely to be a biologic than a project being developed by a startup, which fits the description of many startups as biotechnology companies. Table 1 also contains *Overlap*, which is an indicator among acquired projects for whether the acquiring big firm had another ongoing project in the same ICD-9 as the acquired project at the time of acquisition. For example, if the big firm had a project to treat a type of lymphoid leukemia (ICD-9 204) already in progress when it acquired the startup, who also had a lymphoid leukemia project in progress, then *Overlap* is equal to one. Approximately 58.1% of acquired drugs overlap with the portfolio of the acquirer.

Finally, the last group of variables are the mutually exclusive therapeutic category dummies. 21.5% of projects belong to the "other" category, followed by 18.3% in the oncology category, then by neuroscience and infectious diseases. Startups and big firms have a similar distribution of projects across therapeutic categories though startups tend to have a higher share of projects for infectious diseases and other but fewer for cardiovascular diseases and neuroscience. A more notable exception is that acquired projects are around 10 ppt more likely to be oncology drugs than both non-acquired startups and big firms.

5.2 Evidence on Innovation

The primary measure of innovation here is the number of newly approved projects. To this end, we are interested in the transition probabilities across phases and how acquisition affects these probabilities. Given that project j was acquired by phase k and reached phase k, what is the probability of reaching phase $k+1$ and how does this compare to projects not acquired by phase k? Specifically, we want to compare acquired startups' projects to non-acquired startups' and big firms' projects. To answer this question, I use a Logit regression specification:

$$Pr[y_{jk} = 1|x_{jk}] = F(\beta_{0k} + \beta_{1k}Acquired_{jk} + \beta_{2k}Big_j + x'_j\beta_{3k} + x'_{jk}\beta_{4k}) \quad (1)$$

where F is the Logistic probability distribution, y_{jk} is an indicator equal to one if project j reaches phase $k+1$, $Acquired_{jk}$ is an indicator equal to one if project j is acquired during or before phase k conditional on reaching phase k, Big_j is an indicator equal to one if project j is originated by a big firm, x_j are project-level controls which are constant across all phases, and x_{jk} are project-level controls which vary by phase. All coefficients are phase-specific. Note that $Acquired_{jk}$ may vary over phases within the same project. For example, consider three projects: A, B, and C. Each project reaches at least phase I. Project A is acquired during phase 0, project B is acquired during phase I, and project C is never acquired. In phase 0, project A is an acquired project, while projects B and C are non-acquired projects. In phase I, now both projects A and B are acquired projects while project C remains a non-acquired project. In this way, projects move into the acquisition group as they are acquired during R&D. Together $Acquired_{jk}$ and Big_j create three mutually exclusive groups at each phase k: projects originated by startups that have not been acquired, projects originated by startups that have been acquired, and projects originated by big firms. The excluded group in the regression will be the non-acquired startup projects.

The coefficients of the Logit regressions are given in Table 3. The column titles identify phase k, so column (1) displays the coefficients for the transition probabilities from phase 0 to phase I. The control variables include $Biologic_j$, $LogCompPhasek$, and therapeutic category fixed-effects. It is important to control for therapeutic category fixed effects because the average probability of success differs across categories. Oncology projects in particular, which are represented disproportionately among acquired projects relative to all projects, are generally more difficult to develop treatments for and therefore these projects have a higher likelihood of failure.

The results in Table 3 show that acquired projects are less likely to reach phase I from discovery/preclinical at the 10 % level compared to non-acquired projects. From Table 4,

which contains the marginal effects of the Logit regressions, this coefficient translates to a 3.64 ppt decrease in the transition probability. Acquired projects are also significantly less likely to reach phase II from phase I with a marginal effect of -12.7 ppt. There is no significant difference in the transition probabilities from phase II to phase III. Acquired projects are more likely to enter FDA review from phase III and this coefficient is significant at the 5 percent level. This coefficient translates to a marginal 11.6 ppt increase in the transition probability. Lastly, there is no statistically significant difference in gaining FDA approval, conditional on reaching FDA review. Given that the relationship between acquisition and the transition probability is mixed across phases, how do we interpret the effect of acquisition on innovation or the number of newly approved drugs? Based on the marginal effects of *Acquired* in Table 4, acquired projects 2.9% more likely to reach marketing conditional on entering preclinical development if we use the point estimates for all phases or 4.7% less likely if we use only the statistically significant ones compared to non-acquired projects.

One possible reason for this is that acquired projects are different from non-acquired and big firm projects in ways that have not yet been accounted for, such as the novelty of the project. One way to measure the novelty of a pharmaceutical is through its target-based action. First-in-class projects are defined here as the first approved projects for a particular target-based action.[15] Table A1 presents the Logit phase transition coefficients with one additional variable *FIC*, which is equal to one if no other project with the same target-based action as the focal project has been FDA approved at the beginning of the phase. While being first-in-class is associated with a statistically significant decrease in the transition probability at each phase, controlling for novelty has little effect on the coefficients for *Acquired*. The coefficient for phase 0, which was previously significant at the 10% level, is no longer significant but is similar in magnitude. Therefore, the lower transition probability for earlier-stage projects can not be accounted for using the scientific novelty of the project.

Another possibility is that the transition probabilities are heterogeneous across projects within an acquired startup's portfolio. Recall that the average portfolio of an acquired startup has over six projects and nearly all of these projects are in early development while one or two projects are in phases II, III, or FDA review, which is often the firm's lead project. We can run the same regression again with an additional category *LeadAcquired* as in Table A2. Lead project(s) are defined as the firm's highest phase project(s) at the time of acquisition. Thus, the startup's projects have been partitioned into lead and non-

[15]For example, inotuzumab ozogamicin (Besponsa) was a first-in-class B-lymphocyte cell adhesion molecule inhibitor approved for lymphoid leukemia in 2017.

lead projects, where *LeadAcquired* is equal to one for lead projects. The table does not give a clear story regarding the differential treatment of lead and non-lead projects. In the preclinical phase, there is evidence that lead projects seem to be driving the negative coefficient, while in phase I, the negative coefficient is driven by non-lead projects. There is no evidence for persistent differences in the transition probabilities between lead and non-lead projects, like for example, big pharma shutting down the non-lead projects of acquired startups and focusing on the lead projects.

Competition will affect innovation efforts by all firms. In general, an increase in the number of competing projects at any phase decreases the transition probability of the focal project across all phases. Conditional on reaching the product market, more competing approved projects reduce profits for the focal project, which in turn decreases the expected profits of every project currently in development. A notable exception is that the number of competitors in the next consecutive phase positively affects the transition probability of the focal project, e.g. the number of competitors in phase I as the firm transitions out of phase 0. This suggests that firms may view the number of competing projects in the phase ahead as an indicator or signal of their own potential success in that phase. The other notable exception is the number of competitors in the FDA review stage. Though the number of approved projects negatively affects a firm's transition probabilities at any stage, the number of projects in FDA review may also provide a signal of the focal project's potential success across the entire R&D process.

Can any of the mechanisms mentioned in the introduction of this paper through which acquisition can affect innovation explain these patterns? I attempt to look at each mechanism in isolation in the next two subsections.

5.2.1 Economies of Scale

We first investigate the role of economies of scale and scope by comparing the transition probabilities of projects developed by big firms to non-acquired startups using the variable *Big* in Table 3. Big firms have significantly higher transition probabilities than non-acquired startups for all phases except phase I. In particular, a higher phase II transition probability means that a big firm is more likely to begin phase III conditional on reaching phase II, all else equal. This is what we would expect if big firms had greater financial resources that enabled them to fund expensive phase III trials. Further, a higher FDA approval probability suggests that big firms may benefit from having more experience or greater financial resources dedicated to interacting with the FDA and navigating the regulatory process. Therefore, for a project with the same characteristics, a project developed by big pharma is more likely to be approved than a project developed by a non-acquired

startup.

However, acquired projects do not seem to benefit from big pharma's higher transition rate at these phases. Acquired projects have significantly lower transition rates than big firms for preclinical, phase I, and phase II. Acquired projects have significantly higher transition rates for phase III suggesting that projects in this phase may benefit from economies of scale. An alternative explanation is positive selection into acquisition on project quality because projects in phase III have less risk concerning their safety and efficacy, as they may already have results from pivotal trials and, at a minimum, demonstrated initial signs of safety and efficacy in the preceding phases.

5.2.2 Killer Acquisitions

Next, we investigate the role of the killer acquisition motive on the transition probabilities of acquired projects in Table 5. The regressor of interest is *Overlap* which is an indicator equal to one if the acquirer had an ongoing project in that ICD-9 at the time it acquired the focal project. There is no statistically significant difference in the transition probability in any phase between acquired projects with and without overlap, though the coefficients on preclinical and phase II are negative. The positive but insignificant coefficient on phase III projects provides some suggestive evidence for positive selection on project quality into acquisition at this phase. Big firms who have ongoing projects in a particular ICD-9 are more likely to acquire projects in that ICD-9 that are ultimately successful in phase III, possibly due to their experience with the science and competitive landscape of that particular market. The decrease in sample size for projects acquired in phase III vs. preclinical or phase II makes the interpretation of an insignificant coefficient for *Overlap* more difficult for this phase.

There are several potential explanations for the lack of evidence of killer acquisitions in this data. First, defining markets using the ICD-9 is a considerably more narrow definition than the market definition used in Cunningham et al. (2021).[16] Further, this study uses only a subset of the acquisitions included in their data, which includes acquisitions of firms of all sizes and also asset acquisitions. Indeed, their motivating example of Mallinckrodt acquiring the rights to Synacthen is an asset acquisition. As this study considers only startup acquisitions, the two samples are quite different.

Together, the data suggest that there is persistent negative selection on project quality into acquisition at the preclinical phase, phase I, and phase II that cannot be fully explained by either killer acquisitions, differences in transition probabilities between big firms and

[16]Cunningham et al. (2021) use ATC2 and the mechanism of action listed in their data as their market definition.

startups, observable project characteristics, or the portfolio of the acquired startup. The data also suggests there may be positive selection on project quality at phase III, as the transition probability for acquired projects at this phase is well above the transition probability for big firms. Big firms that have experience in an ICD-9 may be better able to choose target projects in that same ICD-9 that are ultimately successful in phase III, though there is also evidence of economies of scale within the big firm at this phase.

5.3 Evidence on Entry

Acquisitions may not only affect projects already in development, but also on the number of new projects entering development. We can use a multiple-event study framework following Sandler and Sandler (2014) to analyze startup entry into an ICD-9 post-acquisition. The framework is similar to that of a single-event study except that multiple event-time dummies may equal one simultaneously rather than being mutually exclusive. Consider the following specification

$$y_{mt} = \sum_{a=1}^{A_m} \sum_{w=-\tau}^{\tau} \mathbb{1}(t - \tilde{t}_{am} = w)\beta_w + \lambda_m + \gamma_{tz} + \varepsilon_{mt}$$

where a indexes acquisitions, m ICD-9s, t quarters, z potential market sizes, and w the event window. The dependent variable y_{mt} counts the number of new startup projects entering an ICD-9 in a given year-quarter. $\tilde{t}_{am}$ denotes the year-quarter of acquisition a in market m. $z \in \{1, 2, 3\}$ represents the potential market size which corresponds to small, medium, or large, respectively. ICD-9 and calendar time $\times$ market size fixed effects ensure we use variation in the number of entrants within ICD-9 to estimate each β_d while also controlling for any shocks or time trends that affect entry across all ICD-9s within a potential market size category. Lastly, the size of the event window τ is set to five quarters. Because the dependent variable is a nonnegative count, I employ a negative binomial regression model in addition to OLS.

The coefficient estimates of β_w are displayed in Figure 8.[17] The dots represent the point estimates for each coefficient and the bars are 95% confidence intervals. The standard errors are clustered at the ICD-9 level. The specifications for the top left, top right, bottom left, and bottom right graphs respectively are: OLS with ICD-9, market size, and year-quarter fixed effects (FE); OLS with ICD-9 and market size $\times$ year-quarter FE; negative binomial with ICD-9, market size, and year-quarter FE; negative binomial with ICD-9 and market size $\times$ year-quarter FE. The reference line for each graph is equal to the coefficient

[17] The regression results for startup entry are reported in Table A3.

for the quarter immediately preceding the event. I run each specification using both entry by startups and entry by all firms as the dependent variable.

The figure suggests there is a small decline in entry into an ICD-9 by both startups and all firms generally after an acquisition occurs. Figures 1 and 2 provided suggestive evidence that pharmaceutical markets are non-stationary: there is an increasing number of new startups and drugs originated by startups over the sample period. The pre-event coefficients in all graphs appear to be picking up on this trend even with year-quarter FE or market size $\times$ year-quarter FE, as the point estimates are increasing and have confidence intervals that do not include the reference line. This is particularly true for the coefficients for the ends of the event window where the independent variable is the count of the number of events that are more than ± 5 quarters away. Despite the increasing number of entering firms leading up to an acquisition, there is a decline in entry both among startups and among all firms in the quarter the acquisition occurs and for two quarters afterward. Most of these coefficients are just on the margin of statistical significance at the 5% level. The entry count returns to the pre-acquisition level three quarters after the acquisition before dropping again. One potential reason for this trend is the overlap between multiple event windows as big firms acquire several projects in the same ICD-9 in close succession. This is particularly true in oncology markets which a large fraction of the acquired projects belong to.

The results suggest there is a small decrease in entry in the wake of a startup acquisition. One potential reason for this is that the ratio of startups to big firms conditional on the same number of competitors has now increased. There is now an additional competing big firm whose transition probabilities between phases are generally higher than that of a competing startup. However, this analysis does not account for the dynamic equilibrium effect of acquisition on entry, through which the opportunity for acquisition may increase entry among startups. In the remaining sections of the paper, I build and estimate a dynamic model to understand the equilibrium effect of acquisition on entry and innovation.

6 Model

I build a dynamic oligopoly model of the pharmaceutical industry a la Ericson and Pakes (1995). The model will be set in continuous time with an infinite horizon. A Poisson arrival process with govern the timing of moves by each firm. The reference time interval in the model will be a quarter, so the magnitudes of the arrival rates and flow payoffs will be quarterly. The model will endogenize discrete choices regarding drug development,

startup acquisitions, and entry. Firms will receive IID Type 1 Extreme Value private information shocks at every decision, implying Logit choice probabilities. The model will also feature competition, incomplete information, and heterogeneity across firm sizes, therapeutic categories, and market sizes. Selection on drug quality both across the phases of development and into acquisition is captured by the model. Incomplete information implies that firms do not observe the full state, leading us to adopt a moment-based equilibrium concept introduced first by Fershtman and Pakes (2012) and formalized in Ifrach and Weintraub (2016).

6.1 State Variables

Consider an infinite horizon, continuous time model. Let time be indexed by $t \in [0, \infty)$. Firms discount future payoffs according to the continuous discount rate given by ρ. Let markets be indexed by $m = 1, ..., M$ and be independent from one another. For brevity, I will omit the m subscript in what follows unless otherwise necessary. Firms may have at most one project. Hence we index firms/projects by $j = 1, ..., J$. Each project is characterized by a tuple $s_{jt} = (\xi_j, \phi_{jt}, \theta_j)$. ξ_j denotes fixed project quality. Project quality is partially unobserved to the econometrician, though I delay the discussion of this assumption for subsection 6.4. ξ_j is drawn i.i.d. from a Lognormal distribution with mean $\mu_{\xi,z}$ and variance $\varsigma^2_{\xi,z}$ by the firm before entering R&D. Firms observe their own quality draw but not the quality of competing firms. $\phi_{jt} \in \{-1, 1, 2, 3, 4\}$ denotes the drug's current phase of development: discontinuation, phase I of clinical development, phase II, phase III, and approval/marketing, respectively. To reduce the size of the state space and the active number of firms, the preclinical phase is excluded from the model. However, the transition rate from preclinical to phase I is matched to the entry rate. The FDA approval decision will be incorporated as an instantaneous approval probability and fixed cost. Projects are developed by firms with a fixed type $\theta_j \in \{1, 2\}$, representing startups and big firms, respectively. There is also a market-level state vector that firms keep track of $x_m = (y_m, z_m)$. $y_m \in \{1, 2\}$ represents the therapeutic category to which that market belongs, corresponding to not oncology or oncology, respectively. Only two therapeutic categories are allowed to reduce the size of the state space. Oncology markets in particular have transition probabilities that are highly dissimilar from other therapeutic categories. $z_m \in \{1, 2, 3\}$ represents the potential market size which corresponds to small, medium, or large, respectively. The mean and variance of the distribution from which quality is drawn is allowed to vary with market size. The empirical specification of the profit function will be strictly increasing in quality. Therefore, allowing a higher mean for larger market sizes

will translate into higher average profits.

The full state of each market is given by the state of all the projects in the market plus the market-level state: $s_t = (s_{1t}, ..., s_{Jt}, x_m)$. As firms do not observe the quality of competing projects, they cannot observe the full state, which implies that firms have incomplete information. Instead, firms keep track of the full state s_{jt} of their own project, the market-level states, and the phase of other firms $n_t \equiv \{\phi_{-jt}\}$, where $-j$ denotes all firms excluding the focal firm j. Because firms are symmetric, we can restate n_t as

$$n_t = \{n_{\phi t}\}_{\phi \in \{1,2,3,4\}},$$

where $n_{\phi t}$ is the count of firms at phase ϕ at time t. The moment-based state of firm j is therefore defined by $\hat{s}_{jt} = (\xi_j, \phi_{jt}, \theta_j, n_t, x_m)$.

6.2 Drug Development

To advance their project to the product market, firms must invest in costly clinical trials when $\phi_j = \{1, 2, 3\}$. For the duration of each phase, firms pay a fixed flow cost $c_{\phi,\theta,y}$ representing the costs of drug development. This flow cost may vary with the phase, firm type, and therapeutic category to capture differences in R&D costs across the phases of clinical trials, differences in transition probabilities across types, and across therapeutic categories. The phase duration is stochastic and drawn from an exponential distribution with parameter $\lambda_{\phi,x}$. Therefore, the average phase length is given by $1/\lambda_{\phi,x}$. When the end of the phase arrives, firms must make a discrete choice to either advance the project to the next phase of R&D or discontinue the project. This choice is denoted by $d_j^\phi \in \{0, 1\}$, where $d_j^\phi = 1$ implies that the project was advanced to phase $j+1$. Drugs that are discontinued are discontinued forever, earn zero profits, and receive no scrap value. Therefore, the value of discontinuation is normalized to zero. Prior to their decision, firms receive choice-specific, additive, private information shocks drawn from an Extreme Value Type 1 distribution given by $\{\varepsilon_{0j}^\phi, \varepsilon_{1j}^\phi\}$. Firms such that $\phi_j \in \{1, 2\}$ make the following choice:

$$\underset{d_j^\phi \in \{0,1\}}{argmax} \quad \varepsilon_{0j}^\phi \cdot \mathbb{1}(d_j^\phi = 0) + (V(\xi_j, \phi_j + 1, \theta_j, n', x) + \varepsilon_{1j}^\phi) \cdot \mathbb{1}(d_j^\phi = 1), \quad \text{where } n' = n - \mathbb{e}_{\phi_j} + \mathbb{e}_{\phi_j+1}. \tag{2}$$

Here, $\mathbb{e}_\phi$ is a basis vector for the moment space with a one in the entry corresponding to ϕ and zeros in all other entries. Therefore, n' denotes the change in the moment conditional on the firm advancing. V represents the firm's value function, which I will formally derive

in subsection 6.7.2.

6.3 FDA Review

If a firm chooses to advance from phase III of clinical trials, they must receive FDA approval to advance to marketing. FDA approval is modeled as a random, instantaneous draw where the probability of approval is given by ν. The approval decision is denoted by $FDA_j \in \{0, 1\}$, where $FDA_j = 1$ implies that the project was approved. The firm must also pay an instantaneous fixed cost $c_{FDA,\theta,y}$ to take this draw. This fixed cost is allowed to vary by type and therapeutic category and represents any costs to applying for and obtaining FDA approval including the cost of assembling a New Drug Application, communicating with the FDA, providing supplementary data or information, revising labeling information, and conducting and complying with FDA facility inspections. Approved projects automatically proceed to product market competition while rejected projects are discontinued forever. Firms such that $\phi_j = 3$ make the following choice:

$$\underset{d_j^\phi \in \{0,1\}}{argmax} \quad \varepsilon_{0j}^\phi \cdot \mathbb{1}(d_j^\phi = 0) + (\nu \cdot V(\xi_j, \phi_j + 1, \theta_j, n', x) - c_{FDA,\theta,y} + \varepsilon_{1j}^\phi) \cdot \mathbb{1}(d_j^\phi = 1), \tag{3}$$
$$\text{where } \; n' = n - \mathbb{e}_{\phi_j} + \mathbb{e}_{\phi_j+1}.$$

6.4 Product Market Competition

Firms can only profit from projects that are FDA approved with $\phi_j = 4$. Firms receive flow profits $\pi(\xi_j, \theta_j, n, z)$ until the patents for the project expire. Flow profits are a function of the project's quality, the firm's type, the moment, and the potential market size. In particular, the number of competing firms in product market competition will affect flow profits. The duration of patent protection is stochastic and distributed according to an exponential distribution with parameter λ_g. Although firms know exactly when the patents on their project expire, the total patent term is stochastic due to the risk of litigation.[18] When generic entry does occur, I assume the firm's flow profits fall to zero. Generic entry is modeled as though the generic project replaces the branded project. This means that the moment does not change, but the focal firm's profits are affected. However, a project may exit product market competition before or after generic entry due to safety concerns,

[18]The model assumes that patents protect projects, not drugs, which is not the case in reality. Generally, firms have many patents on each drug. Strong patents like the patent on the molecule or active ingredient are very likely to be found valid and infringed in court. Other patents are likely to be more dubious and are used as a strategy to extend a drug's patent protection. These patents are more likely to be challenged by generic firms that are blocked from entering the market (Hemphill & Sampat 2011, 2012). If these patents are found invalid or not infringed, then this may change the term of patent protection for the drug.

lack of demand, or high production costs. The duration of product market competition is determined by an exponential distribution with parameter λ_4.

6.5 Entry

There is a single potential entrant of each type at any given point in time. The arrival rate of entry opportunities is stochastic and distributed according to an exponential with parameter $\lambda_{e,\theta,x}$. The total number of firms for a given phase is bounded above by $J_{\phi,z}$. That is, $n_\phi \leq J_{\phi,z}$. Bounding the total number of firms in each phase at the market size level reduces the size of the state space.[19] We can also think of bounds at the phase level as representing constraints on the number of locations or patients through which clinical trials may be carried out. When $n_1 = J_{1,z}$, $\lambda_{e,1,x}$, $\lambda_{e,2,x} = 0$ so the length of time between entry opportunities is infinite and there is no entry. When the constraint is not binding, $\lambda_{e,1,x}, \lambda_{e,2,x} > 0$. After receiving the opportunity to enter, the potential entrant draws their project quality $\xi_j \sim \text{Lognormal}(\mu_{\xi,z}, \varsigma^2_{\xi,z})$. The potential entrant also receives choice-specific, additive, private information shocks drawn from an Extreme Value Type 1 distribution given by $\{\varepsilon^e_{0j}, \varepsilon^e_{1j}\}$. After observing their quality draw and choice shocks, the firm makes its entry decision $e_j \in \{0, 1\}$, where $e_j = 1$ denotes that the firm chose to enter. Firms that enter do so at phase 1 and do not pay any fixed entry costs. Firms that choose not to enter disappear forever and are replaced by a new potential entrant. Therefore, the potential entrant makes the following choice:

$$\underset{e_j \in \{0,1\}}{argmax} \quad \varepsilon^e_{0j} \cdot \mathbb{1}(e_j = 0) + (V(\xi_j, \phi'_j = 1, \theta_j, n', x) + \varepsilon^e_{1j}) \cdot \mathbb{1}(e_j = 1), \quad \text{where } n' = n + \mathbb{e}_1. \tag{4}$$

6.6 Acquisition

The big firm that is a potential entrant may also enter R&D through the acquisition of a startup. The opportunity to acquire arrives stochastically according to an exponential distribution with parameter $\lambda_{a,x}$. If the opportunity to enter arrives before the opportunity to acquire, then the big firm faces the entry decision described in subsection 6.5. If the opportunity to acquire arrives first, then the big firm faces the acquisition decision described here. Upon the arrival of the acquisition opportunity, the acquirer selects its target startup

[19] Exogenous bounds at the market size-level reduce the number of possible states for smaller markets. However, if a single bound is exogenously imposed on each phase for all market sizes, lower upper bounds would arise endogenously for smaller markets through the profit function, as projects in smaller markets generate lower levels of revenue. As a result, these markets can sustain fewer competitors.

k by taking a uniform draw from all active startups such that $\phi_k \in \{1, 2, 3\}$. The acquirer then observes the target's project quality ξ_k. The acquisition price $p^a_{\phi_k}$ paid by the acquirer to the target is determined using Nash Bargaining. There is also a fixed acquisition cost $c^a_{\phi_k}$ that varies with the phase of the target and must be paid by the big firm if the target is acquired. This fixed cost may represent the cost of due diligence by firms who choose to acquire. The acquirer also receives choice-specific, additive, private information shocks $\{\varepsilon^a_{0j}, \varepsilon^a_{1j}\}$ that are drawn from an Extreme Value Type 1 distribution. A potential entrant big firm that does not acquire disappears forever and is replaced by a new potential entrant big firm. The decision of acquirer j to acquire target k, denoted by $a_{jk} \in \{0, 1\}$ where $a_{jk} = 1$ implies that the acquisition occurred, is given by

$$\underset{a_{jk} \in \{0,1\}}{argmax} \quad \varepsilon^a_{0j} \cdot \mathbb{1}(a_{jk} = 0) + (V(\xi_k, \phi_k, \theta_j = 2, n, x) - p^a_{\phi_k} - c^a_{\phi_k} + \varepsilon^a_{1j}) \cdot \mathbb{1}(a_{jk} = 1) \tag{5}$$

The big firm proposes an acquisition if the value of acquiring exceeds the value of not acquiring. From the perspective of the startup, there is some exogenous probability that they are acquired. The Nash Bargaining problem determining $p^a_{\phi_k}$ is given by

$$\underset{p^a_{\phi_k}}{max} \quad (V(\xi_k, \phi_k, \theta_j = 2, n, x) - p^a_{\phi_k})^{\kappa} \cdot (p^a_{\phi_k} - V(\xi_k, \phi_{\phi_k}, \theta_k = 1, n, x))^{1-\kappa} \tag{6}$$

where κ is the big firm's bargaining power parameter.[20] The first term in parentheses is the big firm's surplus from acquiring, given by the difference in its continuation value with an acquisition minus the acquisition price and its continuation value without an acquisition, which has been normalized to zero. The second term in parentheses is the startup's acquisition surplus which is the acquisition price minus the continuation value without an acquisition. Solving this optimization problem, the acquisition price is equal to

$$p^a_{\phi_k} = (1 - \kappa) \cdot V(\xi_k, \phi_j = 2, \theta_j, n, x) + \kappa \cdot V(\xi_k, \phi_k = 1, \theta_k, n, x) \tag{7}$$

A necessary (but not sufficient) condition for an acquisition to occur is a positive total surplus to be split, $V(\xi_k, \phi_j = 2, \theta_j, n, x) - V(\xi_k, \phi_k = 1, \theta_k, n, x) \geq 0$. While an acquisition does not change the moment faced by firms that are neither the target nor the acquirer, the acquisition rate will still affect third parties through the transition probabilities, which I describe next.

[20] Note that neither the fixed cost of acquisition nor the idiosyncratic shocks enter the Nash Bargaining problem because they are sunk before negotiations begin, though firms are forward-looking regarding the outcome of bargaining.

6.7 Moment-Based Equilibrium

6.7.1 Transitions

The assumption of incomplete information regarding the quality and type of competitors requires adopting an equilibrium concept that is not the Markov Perfect Equilibrium (MPE). Instead, I adopt a moment-based equilibrium concept (Ifrach & Weintraub 2016). Firm strategies and value functions depend on the moment-based state $\hat{s}_{jt}$ instead of the full state s_t. In the model where firms observe the full state of their competitors, an MPE exists and firms use Markov strategies, which create a transition kernel that is a Markov process (see Arcidiacono et al. 2016). However, the dynamics of the moment-based state are not necessarily Markov.[21] To define the equilibrium in moment-based strategies, a Markov approximation of the dynamics of the moment-based state is required. Because firms do not observe the quality or type of their competitors, they must form a belief about the probability that a competing firm takes a given action conditional on the competing firm's phase, the current moment, and the market-level state. I assume this belief is formed by integrating the firms' best response probabilities over their quality and type using the average joint distribution of firm quality and type conditional on the firm's phase, the moment, and the market-level state.

A moment-based strategy for firm j is a mapping from the moment-based state $(\hat{s_j}, \varepsilon_j) \in \hat{S} \times \mathbb{R}^2$ to an action in its choice set,

$$\mathcal{A}_j : (\hat{s_j}, \varepsilon_j) \to \{0, 1\},$$

where $\mathcal{A} = (a, d, e)$ is the firm's acquisition, development, and entry strategies. Given the distribution of the choice shocks, the strategy $\mathcal{A}_j$ implies a response probability for each moment-based state:

$$\sigma^j_{\mathcal{A}}(\hat{s_j}) \equiv Pr[\mathcal{A}_j(\hat{s_j}, \varepsilon_j) = 1 | \hat{s_j}].$$

With Extreme Value Type 1 shocks, the response probabilities are Logit choice probabilities. In equilibrium, we will require that all firms adopt symmetric strategies, so we drop the subscript j on strategies and response probabilities going forward.

[21] Consider a discrete-time capacity competition model where the relevant moment is the sum over the capacity of all competitors. An underlying full state of three competitors each with a capacity of 10 or one competitor with a capacity of 30 has the same moment; the sum over competitors' capacities is 30. But these states do not necessarily yield the same probability distribution for the moment next period. For example, allow firms to make a discrete choice to increase their capacity by one unit next period and assume they pursue this strategy with positive probability. Then with positive probability, the moment next period will be equal to 33 in the model with three firms while the probability of this state transition is necessarily equal to zero in the model with one competitor.

Consider a dataset of observations $\{\hat{s}_{ml}, t_{ml} : m = 1, ..., M, l = 1, ..., L_m\}$ sampled over the time interval $[0, \bar{T}]$ where $\hat{s}_{ml}$ is the vector of firms' moment-based state immediately prior to the l-th non-continuation action in market m and t_{ml} is the time the action is taken. Define the perceived transition probabilities as the average response probability conditional on the phase ϕ, moment n, and market-level state x:

$$\hat{\sigma}_{\mathcal{A}}(\phi, n, x) = \sum_{\theta=1}^{2} \sum_{\xi} \sigma_{\mathcal{A}}(\xi, \phi, \theta, n, x) \cdot \hat{P}[\xi|\phi, \theta, n, x] \cdot \hat{P}[\theta|\phi, n, x], \tag{8}$$

where

$$\hat{P}[\xi|\phi, \theta, n, x] = \underset{\bar{T}\to\infty}{limsup} \frac{\sum_m \sum_l \sum_j \mathbb{1}(\xi_{jml} = \xi, \phi_{jml} = \phi, \theta_{jml} = \theta, n_{ml} = n, x_m = x)}{\sum_m \sum_l \sum_j \mathbb{1}(\phi_{jml} = \phi, \theta_{jml} = \theta, n_{ml} = n, x_m = x)}, \tag{9}$$

$$\hat{P}[\theta|\phi, n, x] = \underset{\bar{T}\to\infty}{limsup} \frac{\sum_m \sum_l \sum_j \mathbb{1}(\theta_{jml} = \theta, \phi_{jml} = \phi, n_{ml} = n, x_m = x)}{\sum_m \sum_l n_{\phi ml} \cdot \mathbb{1}(n_{ml} = n, x_m = x)}. \tag{10}$$

Because firms are symmetric, they can calculate the conditional choice probabilities of their competitors at each moment-based state. Even though a firm cannot observe its competitors' quality or type, they are able to compute the average quality and type distributions in equations (9) and (10) by forward simulation using the choice probabilities for a given initial quality and type distribution. I assume the average quality and type distribution is common knowledge. Intuitively, this reflects the firm's knowledge that competitors in consecutively later stages of R&D will have successively higher quality draws on average and that the distribution of these quality draws will differ by type. The firm uses the average quality and type distributions together with their beliefs about competitors' conditional choice probabilities to calculate the average choice probability unconditional on quality or type in equation (8).

6.7.2 Value Functions

The value functions for each firm are constructed using the perceived transition probabilities and profit function described above. For brevity, only the startup's value functions are presented here.[22] Denote as $V(\hat{s}_j)$ the value of being in the moment-based state $\hat{s}_j$. For

[22]The big firm's value functions are presented in Appendix B.

ease of exposition, define the function which describes changes in the moment n:

$$n'(\phi, \iota_1, \iota_2) = n - \iota_1 \cdot \mathbb{e}_\phi + \iota_2 \cdot \mathbb{e}_{\phi+1}. \tag{11}$$

where $\iota_1, \iota_2 \in \{0, 1\}$.

Following Arcidiacono et al. (2016) and Blevins (2022), I construct the startup's value function for $\phi \in \{1, 2, 3\}$ as:

$$\begin{aligned}
&V(\xi_j, \phi_j, 1, n, x) = \\
&\Bigg(\sum_{\phi=1}^{4} \lambda_{\phi,x} \cdot n_\phi + (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) \\
&\qquad + \lambda_{a,x} \cdot (\Sigma_{\phi=1}^{3} n_\phi \cdot \hat{P}[\theta = 1|\phi, n, x])^{-1} \cdot \sigma_a(\xi_j, \phi_j, 1, n, x) \cdot (1 - \kappa) + \rho\Bigg)^{-1} \\
&\cdot \Bigg(-c_{\phi_j,1,y} + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot (n_\phi - \mathbb{1}(\phi = \phi_j)) \cdot \Big(\hat{\sigma}_d(\phi, n, x) \cdot V(\xi_j, \phi_j, 1, n'(\phi, 1, 1), x) \\
&\qquad + (1 - \hat{\sigma}_d(\phi, n, x)) \cdot V(\xi_j, \phi_j, 1, n'(\phi, 1, 0), x)\Big) \\
&+ \lambda_4 \cdot n_4 \cdot V(\xi_j, \phi_j, 1, n'(4, 1, 0), x) \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) \cdot V(\xi_j, \phi_j, 1, n'(-1, 0, 1), x) \\
&+ \lambda_{a,x} \cdot (\Sigma_{\phi=1}^{3} n_\phi \cdot \hat{P}[\theta = 1|\phi, n, x])^{-1} \cdot \sigma_a(\xi_j, \phi_j, 1, n, x) \cdot (1 - \kappa) \cdot V(\xi_j, \phi_j, 2, n, x) \\
&+ \lambda_{\phi_j,x} \cdot \Big(\gamma + \log\big(1 + \exp\{\nu^{\mathbb{1}(\phi_j=3)} \cdot V(\xi_j, \phi_j + 1, 1, n'(\phi_j, 1, 1), x) - \mathbb{1}(\phi_j = 3) \cdot c_{FDA,1,y}\}\big)\Big)\Bigg)
\end{aligned} \tag{12}$$

The right-hand side of the equation is grouped into six parts and each part begins with a left-justified line. Part one is the discount rate plus the coefficients on the value function of the expected value of no state change. Part two begins with the flow cost of R&D. The remaining portion of part two through part six represent respectively the expected value of a competing firm advancing or discontinuing development, a competing firm exiting the product market, a competing firm entering development, the focal firm being acquired, and the focal firm advancing or discontinuing development. These expected values are determined in general by the product of the value function, the firm strategies or perceived transition probabilities, the number of firms in each phase and of each type, the move arrival rates, and the distribution of the choice shocks.

The startup's value function for $\phi = 4$ is given by:

$$V(\xi_j, 4, 1, n, x) = \left(\sum_{\phi=1}^{4} \lambda_{\phi,x} \cdot n_\phi + (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) + \lambda_g + \rho \right)^{-1}$$
$$\cdot \Bigg(\pi(\xi_j, 1, n_4, z) + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot (n_\phi - \mathbb{1}(\phi = \phi_j)) \cdot \Big(\hat{\sigma}_d(\phi, n, x) \cdot V(\xi_j, \phi_j, 1, n'(\phi, 1, 1), x)$$
$$+ (1 - \hat{\sigma}_d(\phi, n, x)) \cdot V(\xi_j, \phi_j, 1, n'(\phi, 1, 0), x) \Big)$$
$$+ \lambda_4 \cdot (n_4 - 1) \cdot V(\xi_j, \phi_j, 1, n'(4, 1, 0), x)$$
$$+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) \cdot V(\xi_j, \phi_j, 1, n'(-1, 0, 1), x) \Bigg) \tag{13}$$

The parts of this value function have a similar explanation as above except the focal firm now receives flow profits, cannot be acquired by a big firm, and cannot transition to a higher state. The firm's value function is equal to zero upon the arrival of generic entry, captured by λ_g, or the arrival of discontinuation in the product market according to λ_4.

6.7.3 Equilibrium Definition

A moment-based equilibrium is an equilibrium in symmetric moment-based strategies. The strategies $\mathcal{A}(\hat{s_j}, \varepsilon_j) \in \{0, 1\}$ for $\mathcal{A} = \{a, d, e\}$ constitutes a best response if it solves equations (2), (3), (4), or (5), given firm j's moment-based state, beliefs about the strategies of other players, and the model primitives. Following Milgrom and Weber (1985), I characterize the moment-based equilibrium in probability space according to the equilibrium best response probabilities $\sigma_{\mathcal{A}}$. The equilibrium best response probabilities $(\sigma_e, \sigma_d, \sigma_a)$ are a moment-based equilibrium if:

(i) they correspond to the best response strategies satisfying equations (2), (3), (4), and (5), respectively, for all $\hat{s_j} \in \hat{S}$ given the model primitives and that firms play symmetric strategies.

(ii) The beliefs in equation (8) are consistent with the best response probabilities for each $\hat{s_j} \in \hat{S}$.

Ifrach and Weintraub (2016) prove that a moment-based equilibrium always exists for a model in discrete time using an argument similar to Doraszelski and Satterthwaite (2010) and some additional technical conditions to deal with possible discontinuities in the perceived transition kernel in states outside of the recurrent class. I follow this proof to show the existence of the moment-based equilibrium in continuous time in Appendix

C. Although continuous time eliminates multiple equilibria due to simultaneous moves, uniqueness is not guaranteed in general. As a result, we must assume a single MME is played in each moment-based state and that all players expect the same equilibrium to be played at all times both in and out of sample. The algorithm to compute the MME is based on value function iteration with a simulation step to compute the perceived transition kernel. For details, see Appendix D.

7 Estimation

7.1 Identification

The parameters of the model include the discount rate ρ; the rates of state changes $\{\lambda_{e,1,x}, \lambda_{e,2,x}, \lambda_{a,x}, \lambda_{\phi,x}\}_{\phi=1,y=1,z=1}^{4,2,3}$, λ_g; the FDA's approval probability ν; the fixed costs of drug development $\{c_{\phi,\theta,y}\}_{\phi=1,\theta=1,y=1}^{3,2,2}$, $\{c_{FDA,\theta,y}\}_{\theta=1,y=1}^{2,2}$; the fixed acquisition costs $\{c_{\phi}^{a}\}_{\phi=1}^{3}$; the bargaining parameter κ; the initial quality distribution parameters $\{\mu_{\xi,z}, \varsigma_{\xi,z}^{2}\}_{z=1}^{3}$; and the profit parameters ξ, δ_π. In this section, I discuss the modeling assumptions and data which together identify each of these parameters.

We choose a value of the discount rate ρ and assume that all of the model's shocks are distributed according to a Type 1 Extreme Value distribution. We also choose $\lambda_{a,x}$. The acquisition arrival rate cannot be identified from the data because we do not observe when potential acquirers choose not to acquire. This is analogous to choosing the length of a period in a discrete-time model. Assuming that the arrival rate of each phase follows an Exponential distribution and that we observe the start and end date of each phase, $\{\lambda_{e,1,x}, \lambda_{e,2,x}\}_{y=1,z=1}^{2,3}$ are identified from the length of time between consecutive phase end arrivals for preclinical development. The rate parameters $\{\lambda_{\phi,z}\}_{\phi=1,z=1}^{4,8}$ are identified from the inverses of the mean phase lengths. Similarly, λ_g is identified by the inverse of the average time from a project's approval to the time of generic entry. While this parameter can be estimated from the data, I externally calibrate λ_g using estimates of the average length of patent protection available in the literature. The FDA's approval probability ν is identified as the share of firms that receive FDA approval in the data conditional on submitting an NDA. The demand parameters ξ and δ_π are identified using standard arguments for identification in OLS.

Next, we can identify the fixed costs of FDA review $\{c_{FDA,\theta,y}\}_{\theta=1,y=1}^{2,2}$ and the flow costs of development $\{c_{\phi,\theta,y}\}_{\phi=1,\theta=1,y=1}^{3,2,2}$ by backward induction. First note that the perceived transition probabilities $\hat{\sigma}_d(\phi, n, x)$ and $\hat{\sigma}_e(-1, n, x)$ are non-parametrically identified from the transition rate between development phases and the entry rate together with the esti-

mated values of $\{\lambda_{e,1,x}, \lambda_{e,2,x}\}_{y=1,z=1}^{3,2}$, respectively. As a result, every term in equation (13) is identified or observed except for the value function evaluated at each moment-based state. Consider a model with no project quality and therefore no individual unobserved heterogeneity. If there are N_4 total moments such that $\phi = 4$ and θ, x are fixed, then equation (13) implies a system of N_4 equations with N_4 unknowns. There is a unique solution for this system and therefore the phase 4 value function is identified. We can then identify $\{c_{FDA,\theta,y}\}_{\theta=1,y=1}^{2,2}$ using the model-implied development choice probability for phase 3:

$$\sigma_d(3,\theta,n,x) = \frac{\exp\{\nu \cdot V(4,\theta,n'(3,1,1),x) - c_{FDA,\theta,y}\}}{1+\exp\{\nu \cdot V(4,\theta,n'(3,1,1),x) - c_{FDA,\theta,y}\}} \tag{14}$$

Here, $\sigma_d(3,\theta,n,x)$ is non-parametrically identified using the transition rate from phase 3 to FDA review conditional on θ, n, and x. Thus, everything in this equation is identified or observed except $\{c_{FDA,\theta,y}\}_{\theta=1,y=1}^{2,2}$. Intuitively, the fixed cost of FDA review is identified by the transition probability from phase 3 to FDA review conditional on firm type and the therapeutic category. Because $c_{FDA,\theta,y}$ does not vary with project quality, this argument generalizes to the model with individual unobserved heterogeneity.

We can work backward to identify the flow costs of development for each phase. Consider the model-implied development choice probability for phase 2 in a model without individual unobserved heterogeneity:

$$\sigma_d(2,\theta,n,x) = \frac{\exp\{V(3,\theta,n'(2,1,1),x;c_{3,\theta,y})\}}{1+\exp\{V(3,\theta,n'(2,1,1),x;c_{3,\theta,y})\}} \tag{15}$$

In this case, we can identify the phase 3 value functions using the Hotz and Miller (1993) inversion:

$$V(3,\theta,n'(2,1,1),x) = \log\big(\sigma_d(2,\theta,n,x)\big) - \log\big(1-\sigma_d(2,\theta,n,x)\big) \tag{16}$$

Now, we can use equation (12) to identify $c_{3,\theta,y}$ as it is the only remaining term that has not been identified or is observed. The identification of the remaining flow costs is analogous. Intuitively, the transition rate from phase ϕ to phase $\phi+1$ of type θ firms in therapeutic category y identifies $c_{\phi+1,\theta,y}$.

Similar to the flow costs of development, the fixed costs of acquisition are identified using the acquisition probability conditional on the phase of the target. Recall the model-implied acquisition choice probability where the target is in phase ϕ:

$$\sigma_a(\phi,1,n,x) = \frac{\exp\{\kappa \cdot \big(V(\phi,2,n,x) - V(\phi,1,n,x)\big) - c_\phi^a\}}{1+\exp\{\kappa \cdot \big(V(\phi,2,n,x) - V(\phi,1,n,x)\big) - c_\phi^a\}} \tag{17}$$

The Hotz-Miller inversion implies:

$$\kappa \cdot \big(V(\phi, 2, n, x) - V(\phi, 1, n, x)\big) - c^a_\phi = \log\big(\sigma_a(\phi, 1, n, x)\big) - \log\big(1 - \sigma_a(\phi, 1, n, x)\big) \quad (18)$$

Here, the acquisition rate of targets in phase ϕ identifies c^a_ϕ. As with the fixed development costs, because c^a_ϕ does not vary with project quality, this argument generalizes to the model with individual unobserved heterogeneity.

The bargaining parameter is separately identified from the fixed acquisition cost using observed acquisition prices:

$$p^a_{\phi_k} = (1 - \kappa) \cdot V(\phi, 2, n, x) + \kappa \cdot V(\phi, 1, n, x)$$

The only remaining model primitive to be identified are the parameters of the initial quality distribution $\{\mu_{\xi,z}, \varsigma^2_{\xi,z}\}^3_{z=1}$. For projects that reach marketing, we can identify project quality using project fixed effects ξ_{jm} in equation (19). This is a selected sample since we can only identify project quality for projects that reach marketing. We account for this selection process using the model-implied CCPs at each phase in order to identify the parameters of the initial quality distribution.

7.2 Estimation

The model is estimated using a full-solution variant of the maximum likelihood estimation proposed in Arcidiacono et al. (2016) for dynamic games in continuous time. The unobserved heterogeneity in the model prevents us from using a two-step method which does not require solving for the value functions. In an initial step, the profit function, arrival rate parameters, FDA approval probability, and perceived transition probabilities are estimated separately. Next, the maximum likelihood function for the observed sequence of moves is constructed as a function of the model-implied CCPs. Because the model-implied CCPs depend upon the value function, the value function is solved through value function iteration at each evaluation of the maximum likelihood function. Because the perceived transition probabilities can be estimated directly from the data, no simulation is required during the estimation to solve for the value function.

7.2.1 Estimating Profits

The firm's profit is modeled as a reduced-form function of the moment-based state:

$$\pi_j = \xi_j + f(n_4; \delta_\pi) + \varepsilon^\pi_j, \quad (19)$$

where $E[\varepsilon_j^\pi|\hat{s}_j] = 0$, f is a flexible function of the number of competing projects, and δ_π is a vector of parameters. Project quality ξ_j is mapped into the project-specific intercept or fixed effect. In this way, project quality is only partially observable to the econometrician since the project fixed effect can only be identified for projects that reach product market competition. The economic interpretation of project quality is the mean monopoly profit for firm j.

Instead of using a model of consumer demand to derive marginal costs, I use late sample generic prices as a measure of marginal costs. As a result, firm profits can be estimated directly from the discrete-time demand data. Reiffen and Ward (2005) show that market prices begin to approach the long-run marginal cost after significant generic entry occurs. For each molecule, the lowest late sample generic price is used as the estimate of marginal cost for all producers in that molecule. For drugs that did not experience any generic entry during the sample period, the marginal cost is estimated using generic prices for drugs in the same therapeutic class, drug type (biologic vs. small molecule), and product form (pill, liquid, IV, etc.)[23]. We use the estimates of marginal cost to estimate firm profits in a given quarter as $\pi_{jmt} = (p_{jmt} - mc_{jmt}) \times q_{jmt}$, where p is the price, mc is the marginal cost, and q is the quantity for an approved project j in market m in quarter t.

Using the estimate of firm profits, project quality ξ_j and the parameter vector δ_π is estimated using OLS. Denote by $\tilde{\delta}_\pi$ and $\tilde{\xi}$ the estimated profit parameters and project qualities. Denote the predicted value of profits by $\tilde{\pi}$.

7.2.2 Estimating Arrival Rates

The arrival rate parameters $\{\lambda_{\phi,x}\}_{\phi=1,y=1,z=1}^{4,2,3}$ are estimated as the inverse of the observed mean phase lengths within each market-level state. To empirically incorporate the preclinical phase of development into the model, the entry rate parameters $\{\lambda_{e,1,x}, \lambda_{e,2,x}\}_{y=1,z=1}^{2,3}$ are estimating using the arrival rate of the end of preclinical development conditional on firm type and market-level state. $\lambda_{a,x}$ is chosen to be three times the observed acquisition rate conditional on the market-level state. To estimate these parameters and account for cen-

[23]Therapeutic classes for marginal costs are defined using EphMRA codes. I begin by filling in drugs with missing estimates of marginal costs using the mean marginal cost of drugs in the same EphMRA level-4 code. For drugs that are still missing marginal cost estimates at this point, I then use the mean marginal cost of drugs in the same EphMRA level-3 code. This is repeated up to the EphMRA level-1 code. For biologic drugs, lower-cost biosimilars are rare and often do not have prices near marginal cost. For biologics exceeding $100 per standard unit, I assume that marginal costs are $150 per gram. A 2017 Morgan Stanley report estimated the cost of producing biologics at between $95-225 per gram. See https://www.forbes.com/sites/theapothecary/2019/03/08/biologic-medicines-the-biggest-driver-of-rising-drug-prices/?sh=1e23a43f18b0. I then fill in biologics with missing dosage levels using the same methodology as above.

soring of the data, I construct the likelihood function of the observed arrival rates using the assumption of a Poisson arrival process governing the opportunities to move. The data is structured as a sequence of moves taken by firms in each market over time $[0, \bar{T}]$. Let markets be indexed by $m = 1, ..., M$ and moves within a market be indexed by $l = 1, ..., L_m$. Define $\tau_{ml} \equiv t_{ml} - t_{m,l-1}$ to be the time elapsed between the arrival of move opportunities l and $l-1$. Let $(\theta_{ml}, n_{ml}, x_m)$ be the type, moment, and market-level state faced by the firm immediately preceding move l. Let $e_{ml}, d_{\phi ml} \in \{0, 1, -1\}$, $a_{ml} \in \{1, -1\}$ denote the action taken by the firm at move l where -1 implies that the opportunity for such action did not arrive. Let the subscript T denote the final state and time interval after the last action but before $\bar{T}$. The likelihood function is given by

$$\begin{aligned}\mathcal{L} = \prod_{m=1}^{M} \prod_{l=1}^{L_m} \Bigg\{ & \exp\left[-\tau_{ml} \left(\sum_{\phi=1}^{3} n_{\phi ml} \cdot \lambda_{\phi, x_m} + \lambda_{e,1,x_m} + \lambda_{e,2,x_m} + \lambda_{a,x_m} \right) \right] \\ & \times \lambda_{\phi_{ml}, x_m}^{\mathbb{1}\left(d_{\phi ml} \neq -1\right)} \times \times \lambda_{e,\theta_{ml},x_m}^{\mathbb{1}(e_{ml} \neq -1)} \times \lambda_{a,x_m}^{\mathbb{1}(a_{ml} \neq -1)} \\ & \times \exp\left[-\tau_{m_T} \left(\sum_{\phi=1}^{3} n_{\phi mT} \cdot \lambda_{\phi, x_m} + \lambda_{e,1,x_m} + \lambda_{e,2,x_m} + \lambda_{a,x_m}) \right) \right] .\end{aligned}$$

λ_g is externally calibrated using estimates of the length of patent protection in the literature.[24] Specifically, projects have a mean patent protection length of 50 quarters. Denote these estimated rate parameters by $\tilde{\lambda}$.

7.2.3 Estimating Perceived Transitions

The perceived transition probabilities in equilibrium are required to calculate the value function for each guess of the structural parameters. $\hat{\sigma}_e(-1, n, x)$ and $\hat{\sigma}_d(\phi, n, x)$ are estimated for $\phi \in \{1, 2, 3\}$ and for all n, x as a flexible function of the state variables using a Logit regression. The parameters for entry are estimated via the transition rate from preclinical to phase I. Let $\tilde{\sigma}_{\mathcal{A}}(\phi, n, x; \delta_{\phi z})$ denote the reduced-form perceived transition probability where $\delta_{\phi z}$ is a vector of parameters that are phase and market size-specific. Specifically, the perceived transition probabilities are estimated by

$$\tilde{\sigma}_{\mathcal{A}}(\phi, n, x; \delta_{\phi z}) = \frac{\exp(f(n, y, \delta_{\phi z}))}{1 + \exp(f(n, y, \delta_{\phi z}))}.$$

[24] There are many estimates of the length of market exclusivity in the literature. Grabowski and Kyle (2007) estimate a range of 12-15 years. A 2017 journal article from The Commonwealth Fund estimated an average of just over 12 years. See https://www.commonwealthfund.org/publications/journal-article/2017/sep/determinants-market-exclusivity-prescription-drugs-united.

The distribution of firm types in equilibrium conditional on the phase, moment, and market-level state, $\hat{P}[\theta|\phi, n, x]$, is also estimated using a flexible function of the state variables using a Logit regression. Recall that firms do not observe the types of their opponents, so they must form a belief about the share of firms in each phase which are startups or big firms. Let $\tilde{P}[\theta = 1|\phi, n, x]$ denote the reduced-form probability that a firm in phase ϕ while the moment is n and the market-level state is x is a startup, which has the form

$$\tilde{P}[\theta = 1|\phi, n, x; \delta_{\theta\phi z}] = \frac{\exp(f(n, y, \delta_{\theta\phi z}))}{1 + \exp(f(n, y, \delta_{\theta\phi z}))},$$

where $\delta_{\theta\phi z}$ is a vector phase and market size-specific parameters.

The FDA approval probability ν is estimated as the probability that a project is approved conditional on submitting an NDA for FDA review. Denote by $\tilde{\delta}$ the vector of estimated δ parameters and ν.

7.2.4 Estimating Dynamic Parameters

Denote the dynamic parameters by $\mathcal{C} = (\{c_{\phi,\theta,y}\}_{\phi=1,\theta=1,y=1}^{3,2,2}, \{c_{FDA,\theta,y}\}_{\theta=1,y=1}^{2,2}, \{c_{\phi}^{a}\}_{\phi=1}^{3}, \kappa, \{\mu_{\xi,z}\}_{z=1}^{3}, \{\varsigma_{\xi,z}^{2}\}_{z=1}^{3})$. The dynamic parameters are estimated through a nested fixed point algorithm. For each guess of the dynamic parameters, the value functions are solved using value function iteration. No simulation step is required because we have estimated the equilibrium perceived transition probabilities directly from the data. The value functions are used to construct the model-implied conditional choice probabilities of advancing at each phase, entering, and acquiring. The model-implied CCPs are then used to construct the likelihood function for the observed sequence of moves in each market. Because quality ξ_{jm} is not observed for projects that do not reach marketing, the likelihood contribution of these projects is summed over the unobserved project quality. Since each firm's quality is private information, it only enters its own moment-based state and value function. This means that project j's quality only needs to be integrated over project j's contribution to the likelihood.

For simplicity, the log of the project fixed effects are used in the estimation so that the initial quality distribution is Normal. To reduce the number of parameters that need to be estimated, the log project fixed effects are standardized at the market size level. With the distribution of standardized log project fixed effects having mean zero and variance one in each market size, we can treat the fixed effects as a single distribution and estimate a single mean μ_{ξ} and variance ς_{ξ}^{2} for the initial quality distribution. $\{\mu_{\xi,z}\}_{z=1}^{3}, \{\varsigma_{\xi,z}^{2}\}_{z=1}^{3}$ can be backed out by multiplying the estimated initial distribution by the standard deviation and adding the mean of the log project fixed effects within each market size. Denote the

standardized log value of $\tilde{\xi}_{jm}$ by $\tilde{\xi}^*_{jm}$.

The value function can be expressed as a function of the estimated rate parameters, the parameters governing the perceived transition probabilities, the estimated perceived profits, the dynamic parameters, and the moment-based state: $V(\hat{s}_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C})$.The value function is then used to express the model-implied CCPs for development, entry, and acquisition as a function of these objects as well:

$$\sigma_d(\hat{s}_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}; \mathcal{C}) = \frac{\exp\{\tilde{\nu}^{\mathbb{1}(\phi=3)} \cdot V(\hat{s}'_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C}) - \mathbb{1}(\phi = 3) \cdot c_{FDA,\theta,y}\}}{1 + \exp\{\tilde{\nu}^{\mathbb{1}(\phi=3)} \cdot V(\hat{s}'_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C}) - \mathbb{1}(\phi = 3) \cdot c_{FDA,\theta,y}\}},$$

$$\sigma_e(\hat{s}_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}; \mathcal{C}) = \frac{\exp\{V(\hat{s}'_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C})\}}{1 + \exp\{V(\hat{s}'_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C})\}},$$

$$\sigma_a(\hat{s}_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}; \mathcal{C}) = \frac{\exp\{\kappa \cdot \big(V(\hat{s}'_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C}) - V(\hat{s}_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C})\big) - c^a_\phi\}}{1 + \exp\{\kappa \cdot \big(V(\hat{s}'_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C}) - V(\hat{s}_j(\xi^*_j), \tilde{\lambda}, \tilde{\delta}, \tilde{\pi}, \mathcal{C})\big) - c^a_\phi\}},$$

where $\hat{s}'_j$ denotes the new state associated with each choice and ξ^*_j is the firm's standardized log quality. For brevity, I omit the dependence of the CCPs on $\tilde{\lambda}, \tilde{\delta}, \tilde{\pi}$ in what follows.

The likelihood function for the sequence of moves in each market is constructed using the joint likelihood of the next change in any firm's moment-based state occurring after an interval of length τ and being the result of player j taking a non-continuation action, $e_j = 1$, $a_j = 1$, $d_j \in \{0, 1\}$. Let markets be indexed by $m = 1, ..., M$. Let moves within a market be indexed by $l = 1, ..., L_m$ and projects by $j = 1, ..., J_m$. Consider a dataset $\{\hat{s}_{ml}, t_{ml} : m = 1, ..., M, l = 1, ..., L_m\}$ sampled over the time interval $[0, \bar{T}]$ where $\hat{s}_{ml}$ is the vector of firms' moment-based state plus the market-level state immediately prior to the l-th non-continuation action in market m and t_{ml} is the time the action is taken. For approved projects, the moment-based state is known because we have an estimate of the project's quality using $\tilde{\xi}_{jm}$. For projects that do not make it to marketing, we cannot observe the full moment-based state. Define $\tau_{ml} \equiv t_{ml} - t_{m,l-1}$ to be the time between events l and $l - 1$. Let $\mathcal{A}_{jml} \in \{-1, 0, 1\}$ denote the action taken by firm j at move l for $\mathcal{A} \in \{a, d, e\}$. If firm j did not move at l, then $\mathcal{A}_{jml} = -1$. If firm j did move at l, but the move arrival was not for action $\mathcal{A}$, then $\mathcal{A}_{jml} = -1$. Let $\hat{s}_{jml}$ be the moment-based state faced by firm j immediately preceding move l in market m. Let $o_{jm} = 1$ if quality is observed for project j in market m and $o_{jm} = 0$ otherwise. Finally, let $N(\xi^*; \mu_\xi, \varsigma^2_\xi)$ denote the discretized Normal distribution where $\xi^* \in \{\underline{\xi}^*, ..., \bar{\xi}^*\}$. The likelihood function is given by[25]

[25]For a detailed derivation of the likelihood function, see Arcidiacono et al. (2016).

$$
\begin{aligned}
\mathcal{L} = \prod_{m=1}^{M}\prod_{l=1}^{L_m}\Bigg\{ & \exp\left[-\tau_{ml}\cdot\sum_{\theta=1}^{2}\sum_{\xi^*=\underline{\xi}^*}^{\bar{\xi}^*}\lambda_{e,\theta,x_m}\cdot\sigma_e\left(\xi^*,\theta,-1,n_{ml},x_m;\mathcal{C}\right)\cdot N(\xi^*;\mu_\xi,\varsigma_\xi^2)\right]\Bigg\} \\
& \times\prod_{j=1}^{J_m}\Bigg\{\exp\left[-\tau_{ml}\cdot\left(\tilde{\lambda}_{\phi_{jml},x_m}+\mathbb{1}(\theta_{jm}=1,\phi_{jml}<4)\cdot\lambda_{a,x_m}\cdot\left(\Sigma_{\phi=1}^{3}n_{\phi 1ml}\right)^{-1}\cdot\sigma_a\left(\hat{s}_{jml}(\tilde{\xi}_{jm}^*);\mathcal{C}\right)\right)\right] \\
& \times\left(\tilde{\lambda}_{\phi_{jml},x_m}\cdot\sigma_d\left(\hat{s}_{jml}(\tilde{\xi}_{jm}^*);\mathcal{C}\right)\right)^{\mathbb{1}\left(d_{jml}=1\right)}\times\left(\lambda_{e,\theta_{jm},x_m}\cdot\sigma_e\left(\hat{s}_{jml}(\tilde{\xi}_{jm}^*);\mathcal{C}\right)\cdot N(\tilde{\xi}_{jm}^*;\mu_\xi,\varsigma_\xi^2)\right)^{\mathbb{1}\left(e_{jml}=1\right)} \\
& \times\left(\lambda_{a,x_m}\cdot\left(\Sigma_{\phi=1}^{3}n_{\phi 1ml}\right)^{-1}\cdot\sigma_a\left(\hat{s}_{jml}(\tilde{\xi}_{jm}^*);\mathcal{C}\right)\right)^{\mathbb{1}\left(a_{jml}=1\right)}\Bigg\}^{\mathbb{1}\left(o_{jm}=1,\ \phi_{jml}\neq -1\right)} \\
& \times\Bigg\{\sum_{\xi^*=\underline{\xi}^*}^{\bar{\xi}^*}\exp\left[-\tau_{ml}\cdot\left(\tilde{\lambda}_{\phi_{jml},x_m}+\mathbb{1}(\theta_{jm}=1,\phi_{jml}<4)\cdot\lambda_{a,x_m}\cdot\left(\Sigma_{\phi=1}^{3}n_{\phi 1ml}\right)^{-1}\cdot\sigma_a\left(\hat{s}_{jml}(\xi^*);\mathcal{C}\right)\right)\right] \\
& \times\left(\tilde{\lambda}_{\phi_{jml},x_m}\cdot\sigma_d\left(\hat{s}_{jml}(\xi^*);\mathcal{C}\right)\right)^{\mathbb{1}\left(d_{jml}=1\right)}\times\left(\tilde{\lambda}_{\phi_{jml},x_m}\cdot\left(1-\sigma_d\left(\hat{s}_{jml}(\xi^*);\mathcal{C}\right)\right)\right)^{\mathbb{1}\left(d_{jml}=0\right)} \\
& \times\left(\lambda_{e,\theta_{jm},x_m}\cdot\sigma_e\left(\hat{s}_{jml}(\xi^*);\mathcal{C}\right)\cdot N(\xi^*;\mu_\xi,\varsigma_\xi^2)\right)^{\mathbb{1}\left(e_{jml}=1\right)} \\
& \times\left(\lambda_{a,x_m}\cdot\left(\Sigma_{\phi=1}^{3}n_{\phi 1ml}\right)^{-1}\cdot\sigma_a\left(\hat{s}_{jml}(\xi^*);\mathcal{C}\right)\right)^{\mathbb{1}\left(a_{jml}=1\right)}\Bigg\}^{\mathbb{1}\left(o_{jm}=0,\ \phi_{jml}\neq -1\right)} \\
& \times\exp\left[-\tau_{m_T}\cdot\sum_{\theta=1}^{2}\sum_{\xi^*=\underline{\xi}^*}^{\bar{\xi}^*}\lambda_{e,\theta,x_m}\cdot\sigma_e\left(\xi^*,\theta,-1,n_{mT},x_{mT};\mathcal{C}\right)\cdot N(\xi^*;\mu_\xi,\varsigma_\xi^2)\right].
\end{aligned}
$$

We obtain $\mathcal{C}$ as the arg max of the likelihood function over the parameters.

7.2.5 Implementation

I use a grid to approximate the number of competitors in each phase to reduce the size of the state space and keep the estimation and counterfactual simulations tractable. Restricting the maximum number of firms at the phase and market size-level using $J_{\phi,z}$ further reduces the size of the state space because the same grid is used for each market size. In the data, the maximum number of competitors in each phase is increasing in market size. For small markets, the maximum for each phase is 15, 24, 11, and 14, respectively. For medium markets, 40, 57, 20, and 23. Finally, for large markets, 89, 129, 48, and 57. I set $J_{\phi,z}$ for each phase and market size equal to these values plus one such that the maximum number of competitors never binds. These cutoffs are operationalized by adding an exogenous (to the firm) probability that the firm is unable to move to the next phase even if they choose to do so when the state is equal to the highest grid point. I use four grid points per phase

to approximate the number of competitors. This corresponds to four bins where the grid consists of the midpoint of each bin. The bin cutoffs are close to the quartiles of the number of competitors for each phase across all market sizes. However, the exact quartiles are not used in order to reduce the number of states in small and medium markets by taking into account $J_{\phi,z}$.[26] The final cutoffs for the grid are $\{8, 19, 41, 90\}$ for phase I, $\{11, 25, 58, 130\}$ for phase II, $\{5, 12, 21, 49\}$ for phase III, and $\{4, 9, 24, 58\}$ for marketing. These correspond to the $\{25, 50, 81, 100\}$, $\{25, 55, 85, 100\}$, $\{25, 70, 91, 100\}$, and $\{47, 69, 95, 100\}$ percentiles for each phase, respectively. For a more detailed description of the model using the grid approximation and the restriction of the maximum number of firms at the phase and market size level, see Appendix E. Finally, I use seven points to approximate the distribution of standardized log quality ξ^*, $\tilde{\xi}^*_{jm}$: $\{-5, -3, -1, 0, 1, 2, 3\}$.[27] This results in a state space with 50,540 states.

The final sample for the structural estimation (which is the same sample used for the descriptive analysis) contains 40,730 observed state changes across 230 markets. The total number of entrants into preclinical over the sample period for small, medium, and large markets is 114 or fewer, 115 to 391, or 391 and greater, respectively. This market size definition results in 92 small markets, 70 medium markets, and 41 large markets. Examples of small markets include meningococcal meningitis; esophageal, cervical, uterine, and thyroid cancers; sickle-cell anemia and hereditary hemolytic anemias; angina pectoris; renal failure; and uterine endometriosis. Examples of medium markets include stomach, liver, bladder, and kidney cancers; type 1 diabetes; schizophrenia; anxiety and neurotic disorders; epilepsy; migraines; muscular dystrophies; ulcerative colitis; and chronic liver disease and cirrhosis. Examples of large markets include HIV; hepatitis; colon, pancreatic, lung, skin, breast, ovarian, prostate, and brain cancers; type 2 diabetes; obesity; depression; Alzheimer's and other cerebral degenerations; Parkinson's; multiple sclerosis; hypertension; asthma; Crohn's disease; and rheumatoid arthritis. There are 645 acquisitions with 335 in phase I, 226 in phase II, and 61 in phase III.[28] Finally, there are 655 approved projects matched with demand data. Of these projects, 167 are in small markets, 218 in

[26] Consider the following example. Let the cutoff be right-inclusive. Using the cutoffs $\{8, 16, 41, 90\}$ for phase I will result in two possible bins for small markets, three for medium markets, and four for large markets. On the other hand, the cutoffs $\{20, 45, 65, 90\}$ results in one possible bin for small markets, two for medium markets, and four for large markets.

[27] In unreported results, the estimates of the structural parameters are robust to the specification of the quality grid.

[28] Acquisitions undertaken in phase I, II, or III will be the same as those in the descriptive analysis. Because the preclinical phase is absent from the structural model, only projects acquired in the preclinical phase that reached phase I are present. This explains the discrepancy between the number of projects in the descriptive analysis versus the structural model. These projects are modeled as being acquired instantly after entering phase I.

medium, 270 in large. Though acquisition prices are available for a subset of the acquisitions, I assume that the bargaining weight $\kappa = 0.5$.[29] Because the drug demand data is quarterly, the unit time period is normalized to one 91.25 day-quarter. The discount rate ρ is set to 0.0195, which corresponds to a yearly discount factor of 0.925.[30]

8 Results

8.1 First-Stage Estimates

The estimates of the reduced-form profit function are given in Table 6, where the dependent variable is quarterly firm profits in millions of dollars. Profits are modeled as a function of the number of competing approved projects and a project fixed effect. As a result, the project fixed effect (or project quality) is interpreted as the project's monopoly profit. Column (1) simply regresses profits on market size category dummies to show that average firm profits are indeed increasing in the proxy chosen for market size. The average small, medium, and large market project makes \$40.39, \$45.73, and \$50.84 million per quarter, respectively, not controlling for the number of competing projects. In columns (2) and (3), the market size category dummies are dropped and profits are regressed on the number of competing projects and its square.[31] Column (4) instead uses the log number of approved projects. In all specifications, firm profits are decreasing in the number of competitors within the relevant range. The preferred specification in column (3) suggests that one additional competitor leads to a \$2.92 million decrease in quarterly profits but that this decrease is declining in magnitude as the number of competitors increases. In other words, profits are convex in the number of competitors.

The estimated density of project fixed effects, or quality ξ of approved projects, is shown in Figure 9. The left-hand side displays the estimated fixed effects while the right-hand side displays the log fixed effects standardized by market size category. The mean log fixed effects are 3.23, 3.48, and 3.93 for small, medium, and large markets, respectively. The corresponding standard deviations are 1.20, 1.03, and 0.79. The distribution for each market has a lot of mass concentrated at relatively low values of quarterly monopoly profits. Over 95% of firms in the sample have monopoly profits less than \$200 million per quarter and over 85% of firms have monopoly profits less than \$100 million. However,

[29] In later versions, this parameter will be estimated using observed acquisition prices.

[30] The discount factor β and the continuous time discount rate are related by the formula $1/\beta = e^{\rho T}$ where $T = 4$.

[31] In principle, the amount of profit that is competed away by each additional approved project may depend on market size. This specification is not used because the market size-specific competition coefficients are very sensitive to the cutoffs used to create the market size categories.

the distribution features a long right tail of firms with monopoly profits of up to nearly $1 billion per quarter. This is consistent with blockbuster drugs being a key feature of the pharmaceutical industry.[32] It also validates the choice of a Lognormal specification for project quality.

The rate parameter estimates are given in Table F1. The entry rates are similar across therapeutic categories for small and medium markets. The estimates suggest that, on average, approximately 0.45 startups and 0.17 big firms enter the market each quarter in small, non-oncology markets. In other words, a startup enters every 2.23 quarters while big firms enter every 5.90 quarters.[33] In medium non-oncology markets, 1.41 startups and 0.59 big firms enter every quarter. There is more heterogeneity with respect to entry in large markets. In large non-oncology markets, 5.26 startups and 2.35 big firms enter every quarter, on average. These numbers are substantially lower in large oncology markets: only 3.56 startups and 1.34 big firms enter every quarter.

Development phases become longer as the phase increases and tend to be longer in oncology markets. In large non-oncology markets, phase I takes 12.0 quarters, phase II 20.35 quarters, and phase III 25.02 quarters. This amounts to an average time from entry to commercialization of 57.37 quarters or 14.33 years. In large oncology markets, phase I takes 11.22 quarters, phase II 25.74 quarters, and phase III 31.31 quarters, for an average total time of 68.27 quarters or 17.07 years. Exit from marketing or discontinuation is rarely observed in the sample. As a result, the duration of marketing is estimated to be very large at 1000 quarters or 250 years. I externally calibrated the duration of patent protection before generic entry to 50 quarters or 12.5 years.

Lastly, the arrival rate of acquisition opportunities is set equal to three times the estimated observed acquisition rate. As a result, the arrival rate of acquisition opportunities is higher in oncology markets and is increasing in market size. The estimated rates imply there is an observed acquisition every 92.5 quarters in small non-oncology markets, 28.0 quarters in small oncology markets, 43.8 quarters in medium non-oncology markets, 11.8 quarters in medium oncology markets, 10.1 quarters in large non-oncology markets, and 4.8 quarters in large oncology markets.

The Logit regressions used to estimate the perceived transition probabilities are shown in Tables F2 - F4. An indicator for whether the focal firm reached phase $\phi + 1$ conditional on being in phase ϕ is regressed on the number of competing firms in each phase, their squares, an oncology market indicator, and a constant.[34] Coefficients are phase and

[32] Blockbuster drugs are typically defined as drugs that earn more than $1 billion in yearly revenue.

[33] The estimated duration between entries is the inverse of the rate parameter estimate.

[34] The squared number of competing firms in each phase is absent from the regressions for small markets due to collinearity.

market-size specific. Across nearly all of the regressions, the oncology market indicator is highly significant, emphasizing the difference between the transition probabilities in oncology vs. non-oncology markets. Empirically, this provides validation for the choice to allow for different flow R&D costs for oncology vs. non-oncology markets. The Logit regressions for estimating the distribution of firm types in equilibrium are shown in Tables F5 - F7. In this case, the dependent variable is an indicator for whether an active firm is a startup. Recall these regressions are used for firms to estimate the number of active startups available for acquisition conditional on the moment and market-level state. Finally, the estimated probability of FDA approval $\hat{\nu}$ is equal to 0.8689 with a standard error of 0.0093.

8.2 Structural Parameter Estimates

The estimates of the flow costs of R&D, fixed costs of FDA review, and fixed costs of acquisition are given in Table 7.[35] Note that because these are opportunity costs, they do not have to be strictly positive.[36] The flow costs of development imply that the cost of each phase for startups in large, non-oncology markets is $287.96 million for phase I, -$39.11 million for phase II, $175.88 million for phase III, and -$13.04 million for FDA review.[37] Therefore, total R&D costs come out to $411.69 million. In large, oncology markets, the phase-level costs in millions of dollars are $176.32, -$136.34, $262.26, and $260.27, respectively, for a total R&D cost of $562.51 million. For big firms, the costs for each phase in large, non-oncology markets in millions of dollars are $183.24,$9.74, $163.12, -$53.16, respectively. Therefore, the total R&D costs are $302.94. In large oncology markets, these costs are $26.79, -$156.50, $211.54, and $95.44 million, respectively, for total R&D costs of $177.27 million. The estimates suggest that big firms have considerable economies of scale, particularly in phase I, FDA review, and oncology markets. Finally, the fixed costs of acquisition are increasing in the phase of the target firm. The fixed cost of acquiring a phase I firm is approximately $68.51 million, phase II approximately $107.28 million, and phase III approximately $131.14 million.

Figure 10 shows the estimated initial distribution of quality and standardized log quality in black. The blue line plots the estimated distribution of quality for approved projects

[35] At present, there are no estimates of the standard errors. The standard errors will be estimated by block bootstrap at the market level.

[36] The cost in phase $\phi + 1$ adjust to match the transition rate from ϕ, so a high transition rate from phase ϕ will push the cost of phase $\phi + 1$ downward.

[37] To aggregate the flow cost over time, we integrate over the length of the phase taking into account the discount factor, i.e. $\int_0^{\lambda_{\phi,x}^{-1}} c_{\phi,\theta,y} \cdot e^{\rho t} = c_{\phi,\theta,y} \cdot \frac{1}{\rho} \cdot (1 - e^{-\rho \cdot \lambda_{\phi,x}^{-1}})$.

in the data. Note that this estimate differs from the distribution of quality in Figure 9 because the estimated standardized log project fixed effects have been discretized according to the quality grid used in the estimation. The mean of the initial distribution $\hat{\mu}_{\xi^*}$ is estimated to be -3.8194 and the variance $\hat{\varsigma}^2_{\xi^*}$ is 5.8318.[38] This implies that the mean initial quality is \$0.5549, \$0.71113, and \$1.1171 million in small, medium, and large markets, respectively.[39] As expected, the distribution of quality for approved projects in the data has the majority of its mass in the right tail of the initial distribution, showing that firms select on project quality as they move through R&D.

To assess the model's fit, I simulate 500 paths from the zero state for a length of 113 quarters and remove the first 40 quarters. The model is simulated this way to replicate the 73 quarters of data available in the sample. It also captures the non-stationarity of markets in the data by allowing markets to begin small and grow over time.[40]

Figure 11 shows the transition probabilities in the data and the model-implied transition probabilities in equilibrium by firm type and therapeutic category with 95% confidence intervals. The model fits the transition probabilities for both startups and big firms in both therapeutic categories well for entry, phase I, and phase II. The point estimates are nearly identical for these phases except for startups in phase II non-oncology markets and startups entering oncology markets where the model estimate is about 3 and 5 ppt too high, respectively. However, the model is less accurate at predicting the phase III transition rates. For startups, the model point estimates are 7 and 5 ppt too high for non-oncology and oncology markets, respectively. For big firms, the model point estimates are 8 and 4 ppt too low, respectively. The confidence intervals for the phase III transition rate in the data are larger due to attrition that reduces the size of the sample. While the model point estimates for phase III are within the confidence interval in the data for oncology markets, they are not for non-oncology markets, which implies that the estimated fixed costs of FDA review is low for startups and high for big firms. For acquired startups, the model fits the transition rates reasonably well in oncology markets with the model point estimates well within the data confidence intervals. In non-oncology markets, the model overpredicts the transition rate in phase I and II by 16 and 17 ppt, respectively. The phase III transition rate is underestimated by 7 ppt, though the model estimate is within the data confidence interval. The model does not currently seem to be capturing the significant negative selec-

[38] The initial distribution of quality in the right-hand side graph of Figure 10 is not a Normal distribution because we have restricted the grid of points to the integers $\{-5, -3, -1, 0, 1, 2, 3\}$.

[39] This is calculated by adding the mean of the log project fixed effects for a given market size to the estimate of $\hat{\mu}_{\xi^*}$ and taking the exponential.

[40] Ideally, the model would be simulated from the initial state for each market. However, because quality is not observed for projects that do not reach marketing, the exact initial state is unknown.

tion that happens during these phases as documented in Section 5. The small number of acquired projects leads to confidence intervals that are significantly larger than all startups or big firms.

Figure 12 shows the acquisition count per market in the data and the model-implied acquisition count in equilibrium by market size, therapeutic category, and phase with 95% confidence intervals. In general, the model fits the average acquisition counts well across all markets and phases. The model estimate of the number of acquired projects across phases and within each phase is typically within the 95% confidence interval implied by the data. The exception to this is phase II projects in oncology markets. The number of projects acquired in phase I is also consistently underestimated across all markets. However, given that the fixed cost of acquisition is only specific to the phase and not the market size or therapeutic category, the model replicates the data well.

Figure 10 shows the estimated density of quality and standardized log quality for approved projects in the data and implied by the model. The model-implied density fits the shape well but has a mean that is slightly shifted to the right. This is apparent in the right-hand side graph. This leads to a thicker right tail and less mass near zero in the Lognormal distribution on the left.

Using the data simulated from the model, we can look at how the selection process works across phases. Figure 13 shows the model-implied equilibrium density of quality at each phase of development by firm size and therapeutic category. Across all markets, the initial, phase I, and phase II distribution are similar, suggesting that there is little selection on quality during entry and at the end of phase I. Non-oncology markets exhibit a higher degree of selection during these phases than oncology markets, driven by the lower flow R&D costs for oncology markets for phase I and phase II. Startups also have higher selection on quality during these phases due to higher flow R&D costs. It is not until firms choose whether to advance into phase III that significant selection on quality occurs. There is a large reduction in the number of projects with quality draws below -1, particularly in non-oncology markets. The selection effect is again stronger for startups as a result of economies of scale in phase III and FDA review. The final round of selection from phase III to marketing further reduces the number of projects below -1 to near zero. The result is a distribution of quality for approved projects concentrated above -1 with a long left tail. The tail is thicker among big firms due to lower FDA review costs. In contrast to all prior phases, the selection effect for oncology markets is stronger than in non-oncology markets for this phase, leaving less mass in the left tails.

8.3 Counterfactual: Ban Startup Acquisitions

For the first counterfactual, we consider a ban on startup acquisitions and its effect on equilibrium outcomes. This is one extreme measure that the FTC could take to address concerns regarding the acquisition of nascent competitors and the subsequent effect on innovation and market concentration. I operationalize this in the model by setting the arrival rate of acquisition opportunities $\lambda_{a,x}$ equal to zero for all x and simulating the model at the estimated parameters. I simulate 500 paths from the zero state for a length of 113 quarters and remove the first 40 quarters using both the model and counterfactual values for $\lambda_{a,x}$. Because the model currently does not fit the transition rates well for acquired projects in non-oncology markets, I concentrate only on oncology markets in what follows.

The transition probabilities for the model and counterfactual are presented in Figure G1. Note that the panel for acquired startups is removed from the figure because we are considering a counterfactual with no acquisitions. Among startups, the entry rate declines by 6.5 ppt, the phase I and phase II transition rates do not change, and the phase III transition rate increases by 2 ppt. Among big firms, there is no change in the entry and phase I transition rates and a 2.5 ppt decline in the phase II and III transition rates.

Figure G1 aggregates the changes in transition rates across all project qualities. We can compare the quality density at each phase in the counterfactual to the model at the original parameter values. Figure G2 displays the model and counterfactual quality density at each phase by firm size. There is a small increase in the density of high-quality for startups. This is most evident from the distribution for phase III and marketing where the density of low- and mid- quality projects with $\xi^* < 0$ has decreased relative to the density of high-quality projects. Big firms appear to have more pronounced changes in the quality density of their projects despite having changes in their transition probabilities that are lower in magnitude. The density of lower-quality projects increases in phase III. Many of these low-quality projects are dropped in the transition to marketing and the quality density of approved projects increases in mean and decreases in variance.

The equilibrium policy functions can help to explain the changes in the quality densities. In Figures G3 and G4, I take the average over the development policy functions for both the original model and the counterfactual by phase, quality, and firm type, weighting by how often the associated moment and market-level state are visited in each equilibrium. In Figure G3, the average startup entry policy for values of standardized log quality below zero has decreased by nearly 7 ppt. In other words, there is now increased selection on quality during entry. The average policy functions of low-quality projects are more greatly affected by an acquisition ban because they benefit most from acquisitions. The economies of scale enjoyed by big firms will have the largest impact on startups with low-

to mid-quality draws that are unlikely to or just on the margin of advancing to the next phase. This is evident when we compare the phase III policy function for startups to that of big firms in Figure G4: the policy function for low-quality projects is equal to zero among startups but ranges between .027 and .122 for big firms. Despite the higher R&D costs faced by startups, high-quality projects are highly likely to make it to market regardless of which firm type owns it.

There is also a small increase in the phase III transition probabilities for $\xi^* = 0$ of about 3 ppt. Constructing the average counterfactual policy function at the distribution of states for the original model reveals that this small decline is a result of the decrease in competition due to reduced entry.[41] However, the average phase III policy function does not seem to fully explain the increase in the transition rate among startups in this phase. All else equal, the increase in selection at entry will push up the transition probability and increase the density of high-quality startup projects in later phases. We see this in phase III but not in phase I and II. This is because removing the possibility for acquisition will also change the quality density at each phase. It is simplest to see this in phase I, the first phase where an acquisition may occur and where only one round of selection has taken place. If the quality density of startups were uniform in this phase, positive selection on quality into acquisition would increase the transition probability and the density of high-quality projects in phase I in equilibrium with an acquisition ban. Figure G5 shows the average acquisition policy function weighted by how often the associated moment and market-level state are visited in each equilibrium. There is positive selection on quality for all phases of development. Across all phases, a project with the highest quality is 13 to 13.5 ppt more likely to be acquired than a project with the lowest. Returning to the phase I example, in the absence of acquisitions, these high-quality projects will remain as startups.

However, if the quality density of startups is not uniform at phase I, an acquisition ban may actually decrease the transition rate and the density of high-quality projects. This is because all firms are chosen as targets for acquisition with equal probability. Very little selection has taken place at phase I, so the density of low-quality projects is high. As a result, they are likely to be chosen as an acquisition target. The high probability of randomly choosing a low quality firm can overpower the positive selection into acquisition.

[41] This exercise separates the change in the policy functions from the change in the states visited in the counterfactual. If the original model and counterfactual policy functions averaged over the distribution of states for the original model are similar, we can conclude that the change in the average counterfactual policy function is due to a change in the states visited. I confirm that the number of competitors has decreased by looking at the average number of competitors over the simulated path for each phase and market size. The mean number of competitors declined in 11 of the 12 phase-market size pairs.

There is some evidence for this in Figure G6, which shows the quality density of startup and big firm projects overlaid with the quality density of acquired projects in the original model. Though hard to see, the density of acquired projects with $\xi^* = -5$ is larger than for all startup projects. The intuition becomes more complicated for phases II and III due to selection across phases and the differences in selection between firm types conditional on phase.

The lack of change in the startups' phase I and II transition rates suggest the increase in the transition rate due to increased selection at entry are negated by the changes to the quality density in the absence of acquisition. The increase in the phase III transition rate is an agglomeration of the effect of increased selection at entry, the small increase in the policy function at this phase, and the increased density of high-quality projects retained by startups in the absence of acquisitions (see Figure G6). These mechanisms plus the high selection on quality among startups in phase III, where the average policy function for low-quality projects is near zero, results in a higher mean quality of approved projects for startups.

In Figure G4, the big firm's average development policy functions remain unchanged except for a small increase in phase III that is largest for mid-quality projects. How then do we explain the decline in the phase II and III transition rates? Counter to startups, a ban on acquisitions means that high-quality projects that would have become big firm projects now remain as startup projects. We can see this in Figure G6. Acquired projects push up the density of high-quality projects in phase II, III, and marketing among big firms. Without them, the reduction in the number of high-quality projects pushes down the transition probabilities of later phases in equilibrium. The decrease in density of high quality projects in marketing is counteracted by the increase in selection at phase III, resulting in the quality density of approved projects for big firms in Figure G2.

The net effect of the changes in the transition probabilities of startups and big firms on the number of approved projects is shown in Figure 14. The number of approved projects declines across all market sizes, though this decline is fairly small in magnitude and only the decline for medium oncology markets is statistically significant. In this market, the number of approved projects decreased by 1.1 projects or 21.2%. Figure 15 shows the change in the density of standardized log quality of approved projects. The mean increases from 0.7675 to 0.9824 and the variance decreases from 1.7003 to 1.1552. The change in mean is equivalent to a change in the mean monopoly profit in a large market from \$109.68 to \$135.97 million per quarter or a 23.97% increase in profit.

To summarize, a ban on startup acquisitions will have several effects in equilibrium. First, there will be a reduction in entry by low- and mid-quality startups. Acquisition

benefits these firms most because they are more likely to be on the margin of advancing to the next consecutive phase when they face the higher R&D costs of startups. Second, low- and mid-quality projects that make it to phase III and would have otherwise been acquired now face much higher selection at phase III as startups. High-quality projects, on the other hand, are likely to reach marketing regardless of which firm type owns them. The result is that fewer projects reach marketing but the reduction in the number of approved projects is generally small in magnitude. Conditional on reaching marketing, the density of high-quality projects increases.

9 Conclusion

Big pharma is increasingly using acquisitions to fill their R&D pipelines and the proliferation of the biotechnology industry in the last few decades has created a thick market of innovative target startups to choose from. Regulators in several countries, including the FTC in the U.S., are jointly building new guidelines for pharmaceutical mergers, citing concerns regarding the acquisition of nascent competitors on innovation and market structure. This paper seeks to understand the dynamic equilibrium effects of biotech startups acquisitions by big pharma, particularly on entry and innovation by startups.

The empirical strategy to answer this question has two steps. First, I present new descriptive evidence for the relationship between acquisition and the success of acquired startup's projects using a novel dataset combining pharmaceutical R&D data, acquisition data, and pharmaceutical sales data. I find that acquired projects in the early phases of development are persistently negatively selected with success probabilities below both non-acquired startup projects and big firm projects, while projects acquired in phase III are 12 and 5 ppt more likely to successfully complete this phase than these two groups, respectively.

Second, motivated by this evidence, I build a dynamic oligopoly model of the pharmaceutical industry where big firms and startups endogenously choose to engage in project development, startup acquisitions, entry, and exit. Firms select on their fixed project quality at each phase of R&D and into acquisition, allowing higher quality firms to reach later phases of R&D and be more likely acquisition targets. Firms have asymmetric information regarding the quality and size of their competitors, leading to the adoption a moment-based equilibrium concept. The model does well fitting the transition rates across phases, average market-level acquisition counts, and the distribution of quality for approved projects. Currently, the model struggles to fit the negatively selected acquired projects in phase I and II in non-oncology markets.

The main counterfactual of this paper considers a ban on startup acquisitions. The results in the counterfactual are currently confined to oncology markets since the model fits the transition rates of acquired projects well in these markets. The ban will have several effects in equilibrium. First, there will be a reduction in entry by low- and mid-quality startups. These firms are more likely to be on the margin of advancing to the next consecutive phase when they face the higher R&D costs of startups. As a result, they benefit most from the opportunity of being acquired and the lower R&D costs of big firms. Second, low- and mid-quality projects that make it to phase III and would have otherwise been acquired now face much higher selection at phase III as startups. High-quality projects, on the other hand, are likely to reach marketing regardless of which firm type owns them. The result is that fewer projects reach marketing but the reduction in the number of approved projects is generally small in magnitude. Conditional on reaching marketing, the density of high-quality projects increases.

This project directly informs ongoing discussions among regulators at the FTC and in Canada, the U.K., and the E.U. The results of the counterfactual indicate that regulators trade off between the number and the quality of approved drugs when considering limiting startup acquisitions. Going forward, this paper will be adjusted to better fit the persistent negative selection into acquisition in the early phases of R&D in non-oncology markets. One way to do this is to augment the bargaining process such that bargaining is more likely to succeed with low-quality projects, increasing their probability of being acquired. Another potentially more complicated way is to introduce asymmetric information between the target and acquirer as in Samuelson (1984). This can generate negative selection without completely unraveling the acquisition market because, conditional on project quality, projects are worth more to big firms than to startups due to lower R&D costs. Once the model can capture this feature of the data, the counterfactual can be extended to non-oncology markets.

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Tables

Table 1: Startup Project Summary Statistics

	Not Acquired			Acquired			All Startups		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
ReachPhaseI	0.367	0.482	24035	0.344	0.475	489	0.366	0.482	24524
ReachPhaseII	0.785	0.411	7976	0.653	0.477	288	0.780	0.414	8264
ReachPhaseIII	0.332	0.471	4715	0.298	0.458	242	0.330	0.470	4957
ReachFDA	0.438	0.496	1144	0.577	0.497	78	0.447	0.497	1222
ReachMkt	0.834	0.372	435	0.915	0.282	47	0.842	0.365	482
CompPhase0	78.0†	118.0	23620	73.0†	118.5	928	78.0†	118.0	24548
CompPhaseI	20.0†	19.4	24274	25.7†	18.9	948	20.0†	19.4	25222
CompPhaseII	19.0†	22.9	24926	26.3†	24.9	964	19.5†	23.0	25890
CompPhaseIII	6.0†	6.8	25096	7.7†	6.9	967	6.0†	6.8	26063
CompFDA	1.0†	2.1	25130	1.0†	2.0	967	1.0†	2.1	26097
CompMkt	5.0†	9.2	25224	6.5†	9.4	967	5.0†	9.2	26191
Biologic	0.400	0.490	33253	0.349	0.477	1096	0.399	0.490	34349
Overlap				0.581	0.494	1096			
Infectious	0.141	0.348	33253	0.120	0.325	1096	0.140	0.347	34349
Oncology	0.184	0.387	33253	0.286	0.452	1096	0.187	0.390	34349
Metabolic	0.095	0.294	33253	0.077	0.266	1096	0.095	0.293	34349
Cardiovascular	0.085	0.279	33253	0.100	0.301	1096	0.086	0.280	34349
Neuroscience	0.139	0.346	33253	0.098	0.297	1096	0.138	0.345	34349
Respiratory	0.048	0.213	33253	0.079	0.270	1096	0.049	0.215	34349
Immunology	0.079	0.269	33253	0.079	0.270	1096	0.079	0.269	34349
Other	0.229	0.420	33253	0.161	0.367	1096	0.227	0.419	34349

Startup project summary statistics by acquisition status for 2000 - 2018.
†Median displayed instead of mean.

Table 2: All Project Summary Statistics

	Startups			Big Firms			All Firms		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
ReachPhaseI	0.366	0.482	24524	0.540	0.498	10415	0.418	0.493	34939
ReachPhaseII	0.780	0.414	8264	0.739	0.439	5576	0.764	0.425	13840
ReachPhaseIII	0.330	0.470	4957	0.381	0.486	3914	0.353	0.478	8871
ReachFDA	0.447	0.497	1222	0.533	0.499	1501	0.494	0.500	2723
ReachMkt	0.842	0.365	482	0.884	0.320	837	0.869	0.338	1319
CompPhase0	78.0†	118.0	24524	73.0†	109.9	10415	76.0†	115.7	34939
CompPhaseI	20.0†	19.3	25198	21.0†	19.0	10955	20.3†	19.3	36153
CompPhaseII	19.3†	23.0	25863	19.0†	22.7	11565	19.0†	22.9	37428
CompPhaseIII	6.0†	6.8	26035	6.0†	6.7	11875	6.0†	6.8	37910
CompFDA	1.0†	2.1	26068	1.0†	2.0	11961	1.0†	2.0	38029
CompMkt	5.0†	9.2	26162	5.0†	8.8	12255	5.0†	9.1	38417
Biologic	0.399	0.490	34320	0.203	0.403	13084	0.345	0.475	47404
Infectious	0.140	0.347	34320	0.113	0.317	13084	0.133	0.339	47404
Oncology	0.187	0.390	34320	0.173	0.378	13084	0.183	0.387	47404
Metabolic	0.095	0.293	34320	0.105	0.306	13084	0.097	0.297	47404
Cardiovascular	0.086	0.280	34320	0.118	0.322	13084	0.095	0.293	47404
Neuroscience	0.138	0.345	34320	0.162	0.368	13084	0.145	0.352	47404
Respiratory	0.049	0.215	34320	0.066	0.248	13084	0.053	0.225	47404
Immunology	0.079	0.269	34320	0.079	0.269	13084	0.079	0.269	47404
Other	0.226	0.419	34320	0.185	0.388	13084	0.215	0.411	47404

Project summary statistics by firm size for 2000 - 2018.
†Median displayed instead of mean.

Table 3: Logit Phase Transition Coefficients

	(1) Phase 0	(2) Phase I	(3) Phase II	(4) Phase III	(5) FDA
Acquired	-0.182*	-0.762***	-0.0253	0.657**	0.734
	(0.106)	(0.135)	(0.151)	(0.280)	(0.549)
Big	0.762***	-0.245***	0.219***	0.352***	0.350**
	(0.0266)	(0.0434)	(0.0485)	(0.0954)	(0.176)
Biologic	0.206***	0.0273	0.0600	-0.166	0.212
	(0.0266)	(0.0463)	(0.0523)	(0.107)	(0.204)
LogCompPhase0	-1.216***	-0.523***	-0.0672	-0.246***	0.0213
	(0.0253)	(0.0433)	(0.0470)	(0.0844)	(0.154)
LogCompPhaseI	1.087***	-0.289***	-0.181***	-0.0181	-0.00758
	(0.0366)	(0.0599)	(0.0633)	(0.116)	(0.209)
LogCompPhaseII	-0.00458	0.748***	-0.890***	-0.364***	-0.554***
	(0.0283)	(0.0541)	(0.0592)	(0.106)	(0.210)
LogCompPhaseIII	0.191***	-0.00672	1.258***	-0.410***	-0.0103
	(0.0272)	(0.0483)	(0.0614)	(0.103)	(0.190)
LogCompFDA	0.0789***	0.0489	0.123***	2.552***	0.303*
	(0.0235)	(0.0403)	(0.0461)	(0.113)	(0.160)
LogCompMkt	-0.240***	-0.249***	-0.166***	-0.259***	0.272*
	(0.0193)	(0.0337)	(0.0364)	(0.0707)	(0.151)
Constant	1.389***	2.512***	0.656***	0.807***	2.408***
	(0.0727)	(0.133)	(0.136)	(0.240)	(0.464)
Therap. Cat. FE	Y	Y	Y	Y	Y
N	34939	13840	8871	2723	1319
Pseudo-R^2	0.141	0.067	0.082	0.239	0.036

Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 4: Logit Phase Transition Marginal Effects

	(1) Phase 0	(2) Phase I	(3) Phase II	(4) Phase III	(5) FDA
Acquired	-0.0364*	-0.127***	-0.00518	0.116**	0.0813
	(0.0212)	(0.0225)	(0.0308)	(0.0492)	(0.0608)
Big	0.152***	-0.0410***	0.0447***	0.0621***	0.0388**
	(0.00508)	(0.00723)	(0.00988)	(0.0167)	(0.0195)
Biologic	0.0410***	0.00456	0.0123	-0.0292	0.0234
	(0.00529)	(0.00774)	(0.0107)	(0.0188)	(0.0226)
LogCompPhase0	-0.242***	-0.0874***	-0.0137	-0.0433***	0.00236
	(0.00444)	(0.00713)	(0.00961)	(0.0148)	(0.0171)
LogCompPhaseI	0.217***	-0.0483***	-0.0371***	-0.00319	-0.000839
	(0.00696)	(0.00999)	(0.0129)	(0.0204)	(0.0231)
LogCompPhaseII	-0.000913	0.125***	-0.182***	-0.0642***	-0.0614***
	(0.00564)	(0.00885)	(0.0115)	(0.0186)	(0.0233)
LogCompPhaseIII	0.0380***	-0.00112	0.257***	-0.0722***	-0.00114
	(0.00541)	(0.00808)	(0.0115)	(0.0180)	(0.0211)
LogCompFDA	0.0157***	0.00817	0.0251***	0.450***	0.0336*
	(0.00468)	(0.00674)	(0.00942)	(0.0118)	(0.0177)
LogCompMkt	-0.0478***	-0.0417***	-0.0339***	-0.0456***	0.0301*
	(0.00381)	(0.00561)	(0.00741)	(0.0124)	(0.0167)
N	34939	13840	8871	2723	1319

Marginal effects of Logit regression where the dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 5: Logit Phase Transition Coefficients - Killer Acquisitions

	(1) Phase 0	(2) Phase I	(3) Phase II	(4) Phase III	(5) FDA
Acquired	-0.0690	-0.819***	0.181	0.206	0.564
	(0.164)	(0.209)	(0.222)	(0.404)	(0.768)
Overlap	-0.193	0.0947	-0.366	0.827	0.318
	(0.214)	(0.268)	(0.296)	(0.542)	(1.068)
Big	0.762***	-0.245***	0.219***	0.352***	0.351**
	(0.0266)	(0.0434)	(0.0485)	(0.0954)	(0.176)
Biologic	0.206***	0.0272	0.0597	-0.163	0.212
	(0.0266)	(0.0463)	(0.0523)	(0.107)	(0.204)
LogCompPhase0	-1.216***	-0.523***	-0.0675	-0.249***	0.0200
	(0.0253)	(0.0433)	(0.0470)	(0.0845)	(0.155)
LogCompPhaseI	1.088***	-0.289***	-0.178***	-0.0206	-0.00860
	(0.0366)	(0.0599)	(0.0633)	(0.116)	(0.209)
LogCompPhaseII	-0.00476	0.748***	-0.891***	-0.365***	-0.553***
	(0.0283)	(0.0541)	(0.0592)	(0.107)	(0.210)
LogCompPhaseIII	0.191***	-0.00659	1.258***	-0.407***	-0.00945
	(0.0272)	(0.0483)	(0.0614)	(0.103)	(0.190)
LogCompFDA	0.0791***	0.0486	0.123***	2.554***	0.305*
	(0.0235)	(0.0403)	(0.0461)	(0.113)	(0.160)
LogCompMkt	-0.240***	-0.249***	-0.166***	-0.261***	0.269*
	(0.0193)	(0.0337)	(0.0364)	(0.0707)	(0.151)
Constant	1.388***	2.512***	0.653***	0.818***	2.413***
	(0.0727)	(0.133)	(0.136)	(0.240)	(0.465)
Therap. Cat. FE	Y	Y	Y	Y	Y
N	34939	13840	8871	2723	1319
Pseudo-R^2	0.141	0.067	0.082	0.240	0.036

Overlap is equal to one if the acquirer had an ongoing drug project in the same market as the acquired project. Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 6: Profit Estimates

	(1) Profit	(2) Profit	(3) Profit	(4) Profit
Small	40.39***			
	(1.098)			
Medium	45.73***			
	(0.807)			
Large	50.84***			
	(0.925)			
CompMkt		-1.645***	-2.919***	
		(0.196)	(0.367)	
CompMkt^2			0.0302***	
			(0.00570)	
LogCompMkt				-10.55***
				(1.477)
Project FE	N	Y	Y	Y
N	29945	29945	29945	29945
R^2	0.196	0.800	0.800	0.799

Dependent variable is firm profits in millions of dollars. OLS regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 7: Flow and Fixed Cost Parameter Estimates

	Parameter				
Phase ϕ	$c_{\phi,1,1}$	$c_{\phi,2,1}$	$c_{\phi,1,2}$	$c_{\phi,2,2}$	c^a_ϕ
Phase 1	0.2692	0.1713	0.1750	0.0266	0.6851
	()	()	()	()	()
Phase 2	-0.0233	0.0058	-0.0674	-0.0773	1.0728
	()	()	()	()	()
Phase 3	0.0888	0.0824	0.1119	0.1045	1.3114
	()	()	()	()	()
FDA	-0.1304	-0.5316	2.6027	0.9544	
	()	()	()	()	

The flow costs of development are denoted $c_{\phi,\theta,y}$. The fixed costs of FDA review are denoted $c_{FDA,\theta,y}$. All costs are in hundreds of millions of dollars.

Figures

Figure 1: New Startups by Year



Source: Cortellis. *Notes:* New startups are defined as startups that show up in Cortellis for the first time as a firm sponsoring the development of a project. For the precise definition of a startup, see subsection 4.1.

Figure 2: Drugs Originated by Big Pharma and Startups by Year



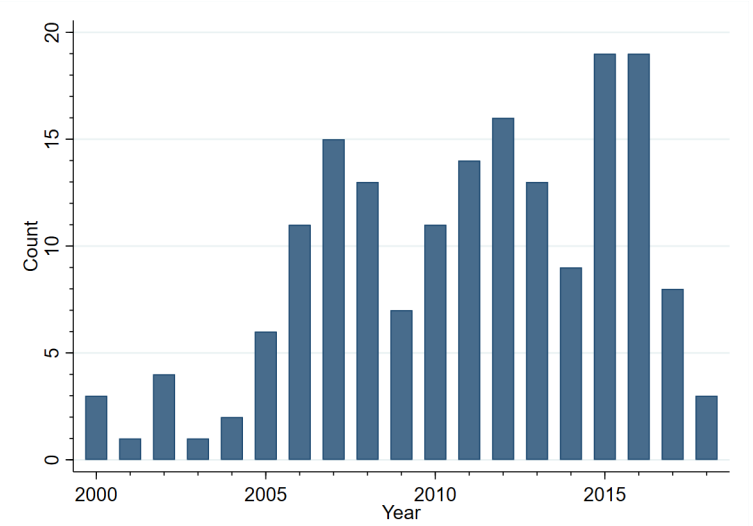
Source: Cortellis. *Notes:* Y-axis counts the number of projects that originated in a given year whose discovery can be attributed to startups or big pharma firms. The sample excludes drugs never developed by a for-profit pharmaceutical firm. The origination year is the first year that the drug shows up in Cortellis for drug discovery/preclinical development. For the precise definition of a startup and a big pharma firm, see subsection 4.1.

Figure 3: Share of Drugs Originated by Startups by Year



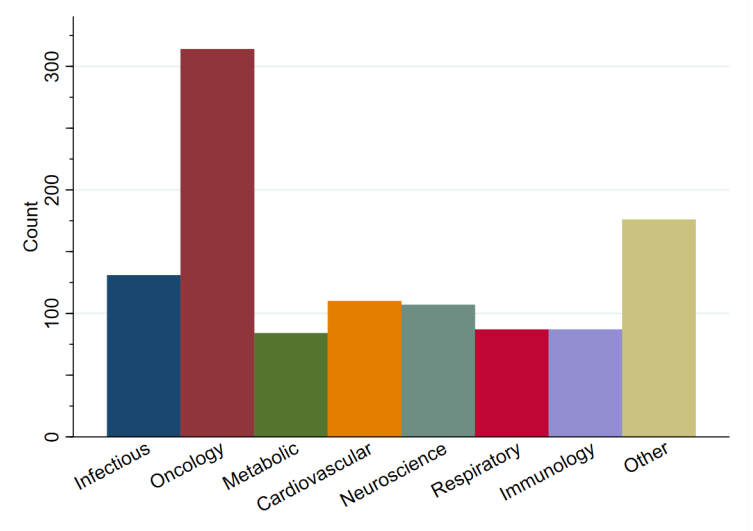
Source: Cortellis. *Notes:* Y-axis provides the fraction of drugs that originated in a given year whose discovery can be attributed to startup. The sample excludes drugs never developed by a for-profit pharmaceutical firm. The origination year is the first year that the drug shows up in Cortellis for drug discovery/preclinical development. For the precise definition of a startup, see subsection 4.1.

Figure 4: Acquisition Count By Year



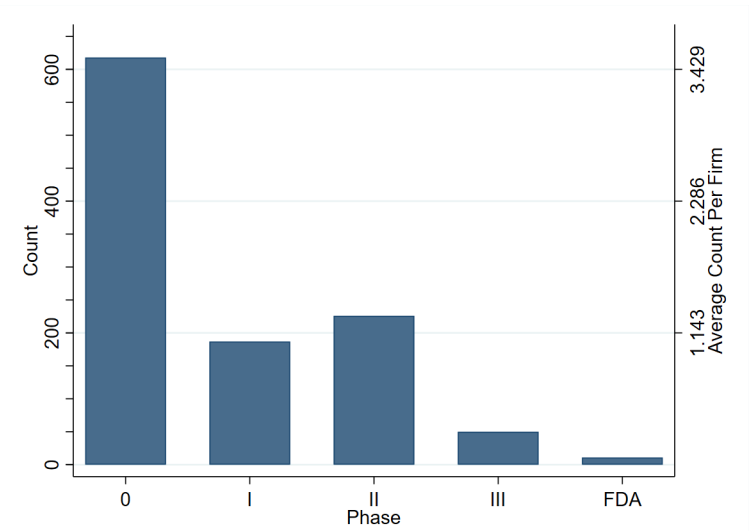
Source: Cortellis and SDC Platinum. *Notes:* Y-axis counts the number of startups acquired in a given year. An acquired startup must have an ongoing project in Cortellis at the time of acquisition (an acquired project) to qualify as an acquired startup.

Figure 5: Acquired Projects by Therapeutic Category



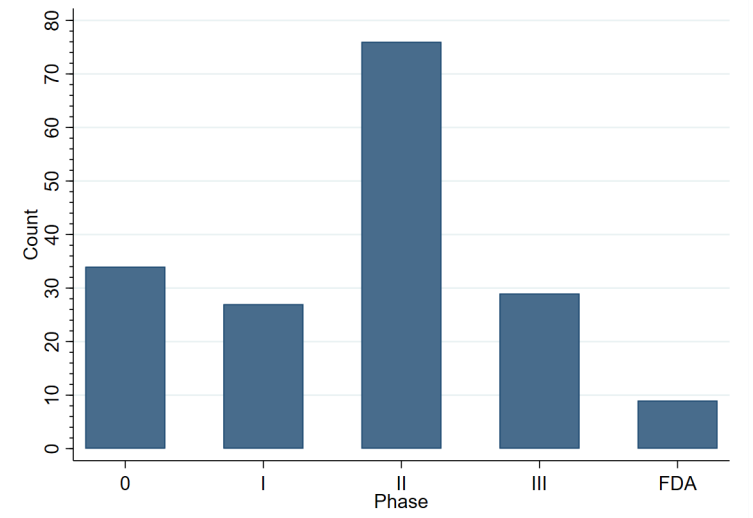
Source: Cortellis and SDC Platinum.

Figure 6: Phase of Acquired Projects at Acquisition



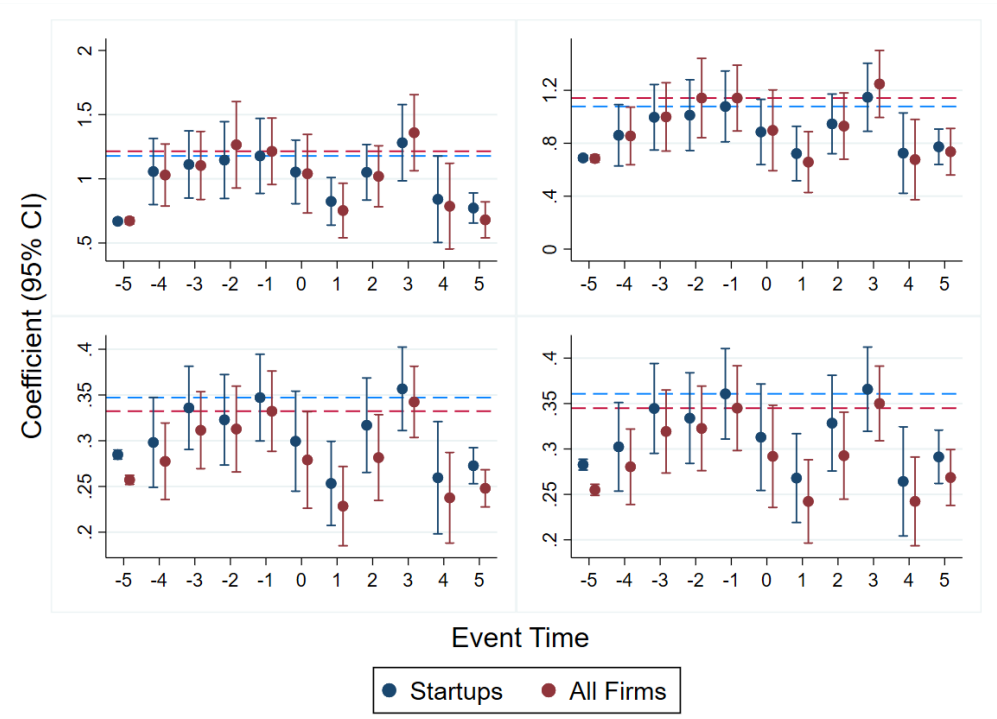
Source: Cortellis and SDC Platinum. *Notes:* The left-hand side y-axis provides the count of acquired projects by the phase at the time of acquisition. The right-hand side y-axis divides the count of projects in each phase by the total number of acquired firms to give the "average portfolio" of an acquired firm. Phase 0 refers to drug discovery and preclinical development while FDA refers to FDA review.

Figure 7: Startup's Highest Phase Project at Acquisition



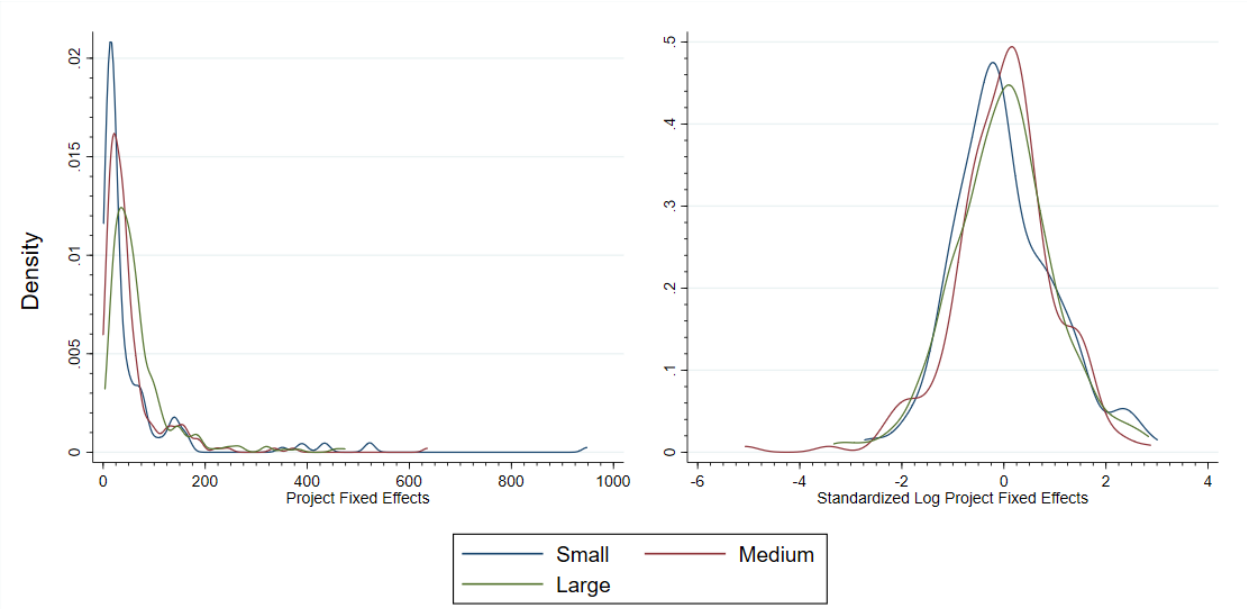
Source: Cortellis and SDC Platinum. *Notes:* The y-axis provides the count of firms whose highest phase project at the time of acquisition belonged to that phase. Phase 0 refers to drug discovery and preclinical development while FDA refers to FDA review.

Figure 8: Entry Event Study



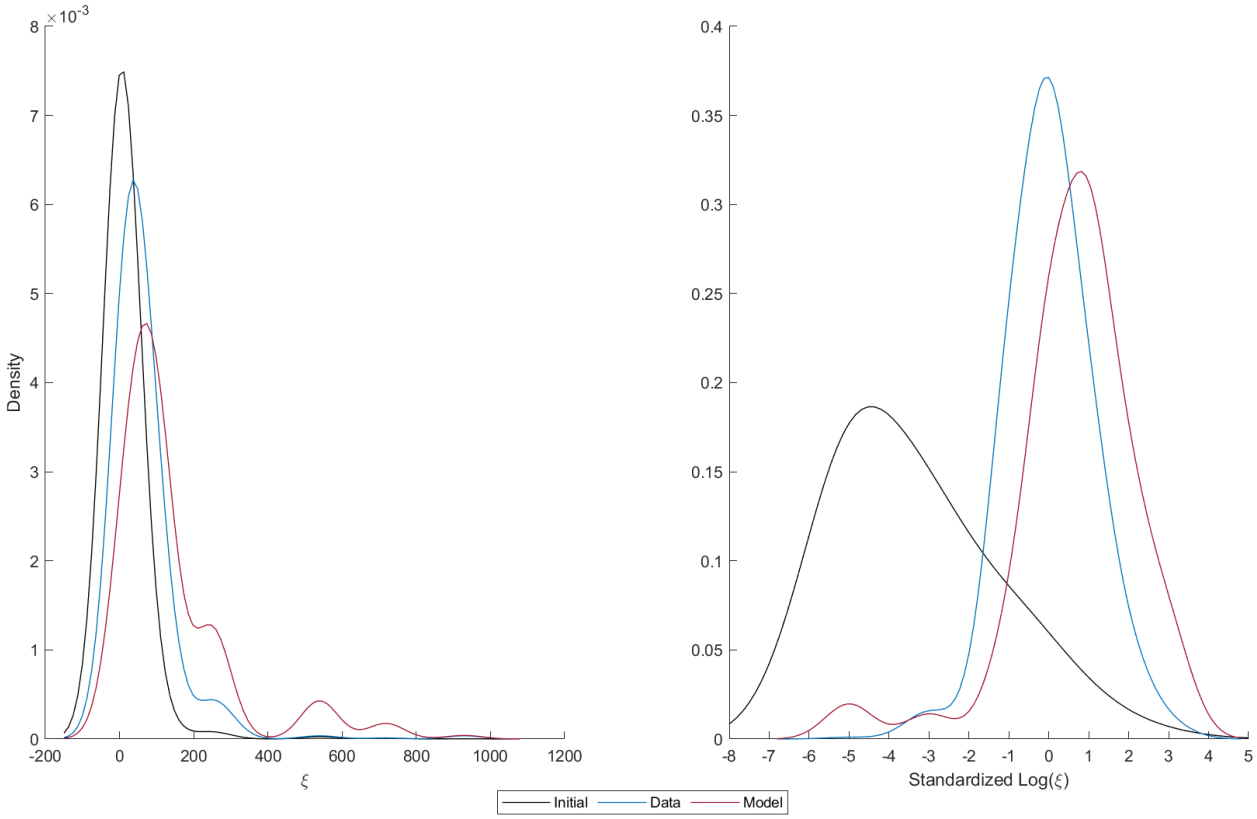
Source: Cortellis and SDC Platinum. *Notes:* Dots are the coefficient point estimate for the event window and bars are the 95% confidence intervals for the entry event study with standard errors clustered at the ICD-9 level. Dependent variable is the count of new entrants into the preclinical phase per market-quarter. The coefficient reference line is equal to the coefficient estimate for event time -1. *Top left:* OLS with ICD-9, market size, and year-quarter FE. *Top right:* OLS with ICD-9 and market size $\times$ year-quarter FE. *Bottom left:* negative binomial with ICD-9, market size, and year-quarter FE. *Bottom right:* negative binomial with ICD-9 and market size $\times$ year-quarter FE.

Figure 9: Density of Quality Estimates for Approved Projects



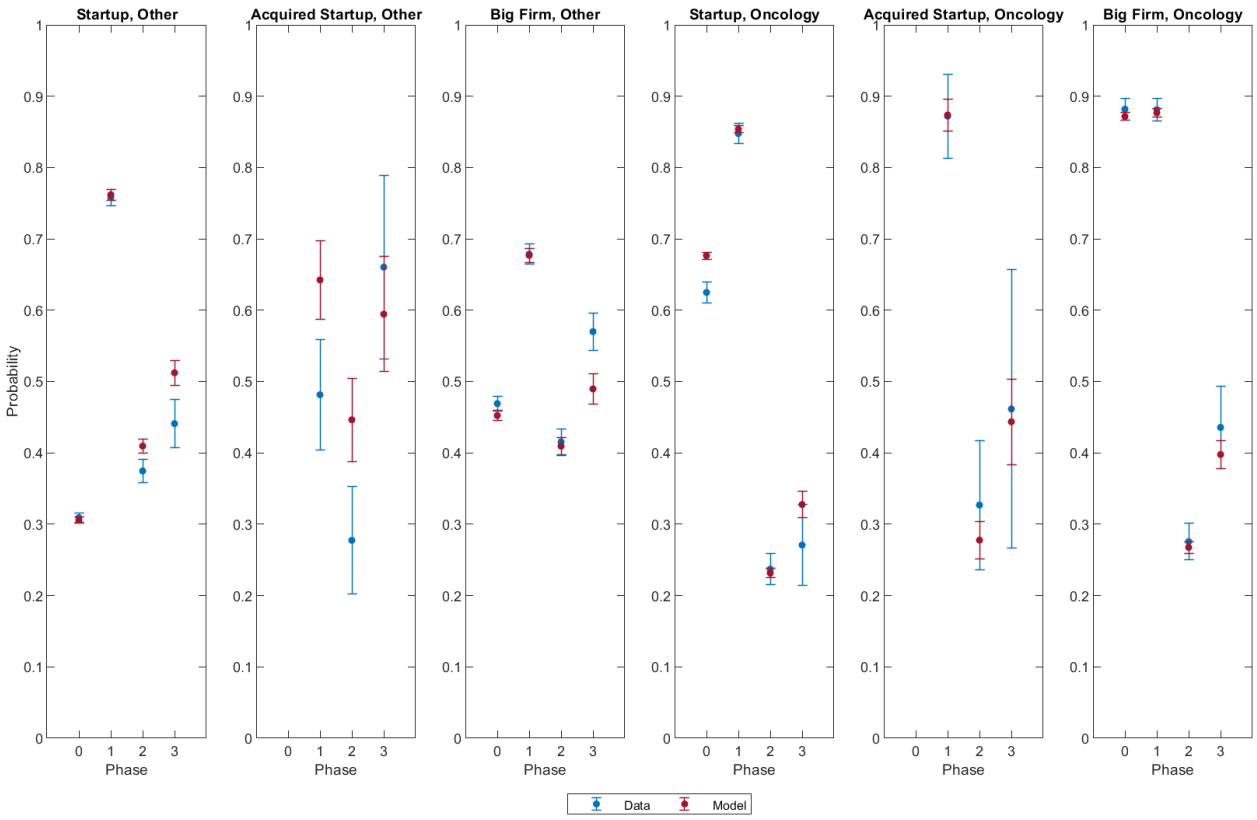
Notes: Left: Kernel density of project quality by market size category. Estimates of project quality ξ are given by project fixed effects from the profit function regression. See column (3) of Table 6 for specification. Project fixed effects are a project's average monopoly profits. *Right:* Kernel density of log project quality standardized within market size category.

Figure 10: Estimate & Model Fit - Distribution of Project Quality



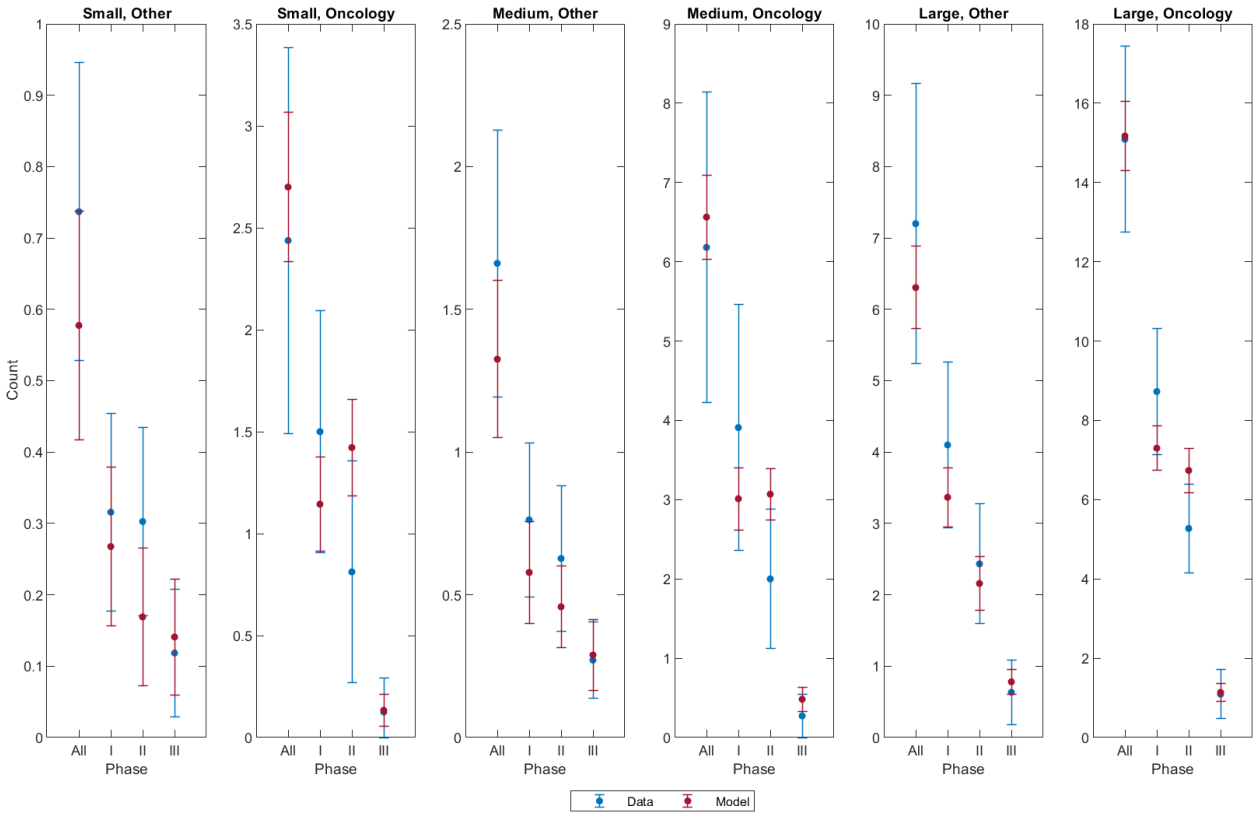
Notes: Left: Kernel density of project quality. *Right:* Kernel density of log project quality standardized within market category. *Black*: Estimated initial distribution of quality. *Blue*: Estimated distribution of quality for approved projects from the data. Also see Figure 9. *Red*: Simulated distribution of quality for approved projects from the model. Model estimates based on 500 model simulations for 113 quarters, removing first 40 quarters.

Figure 11: Model Fit - Transition Probabilities



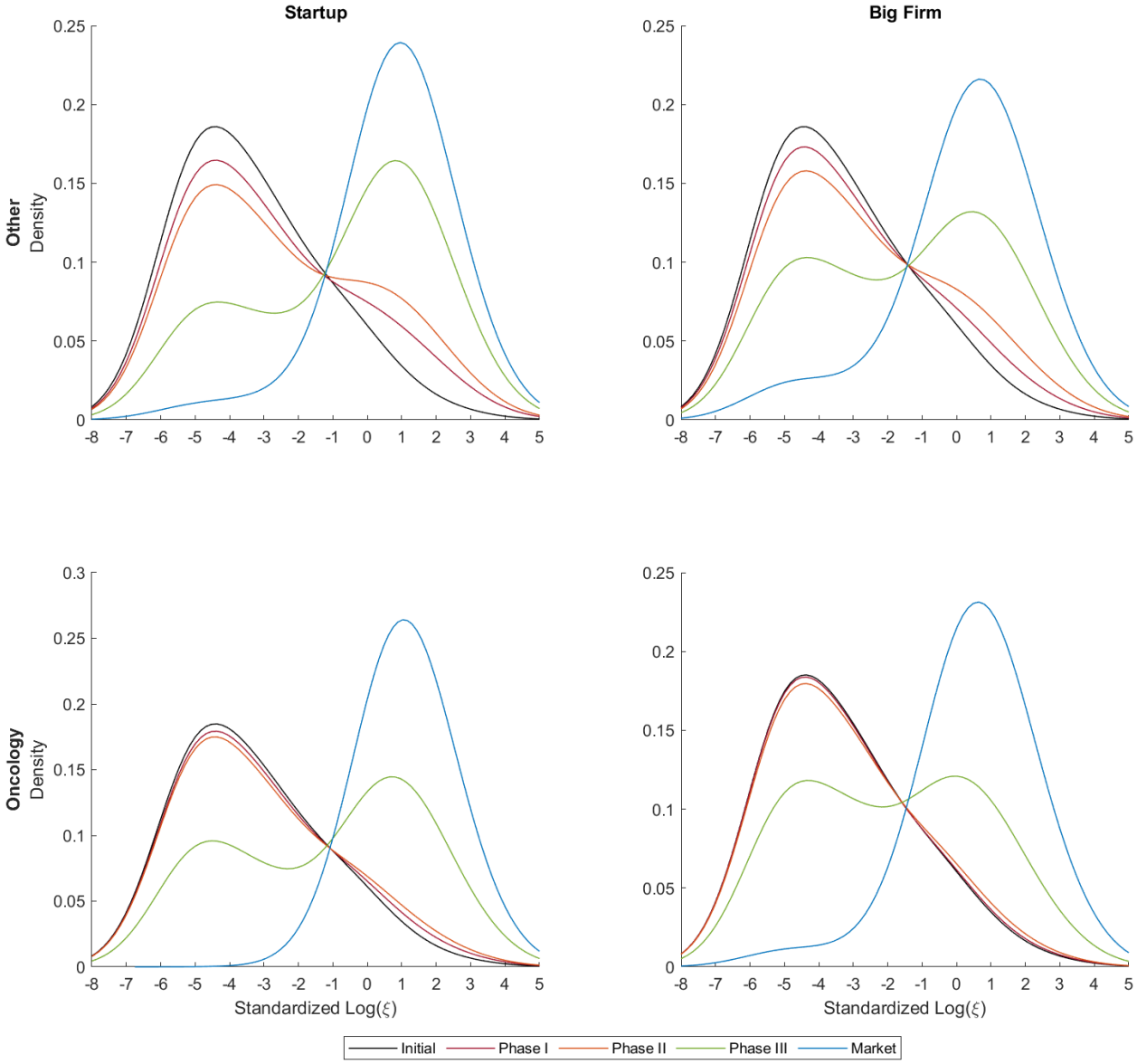
Notes: Dots are the point estimates for the transition probabilities by phase, firm type, therapeutic category. The bars are the 95% confidence intervals. Model estimates based on 500 model simulations for 113 quarters, removing first 40 quarters.

Figure 12: Model Fit - Acquisition Counts



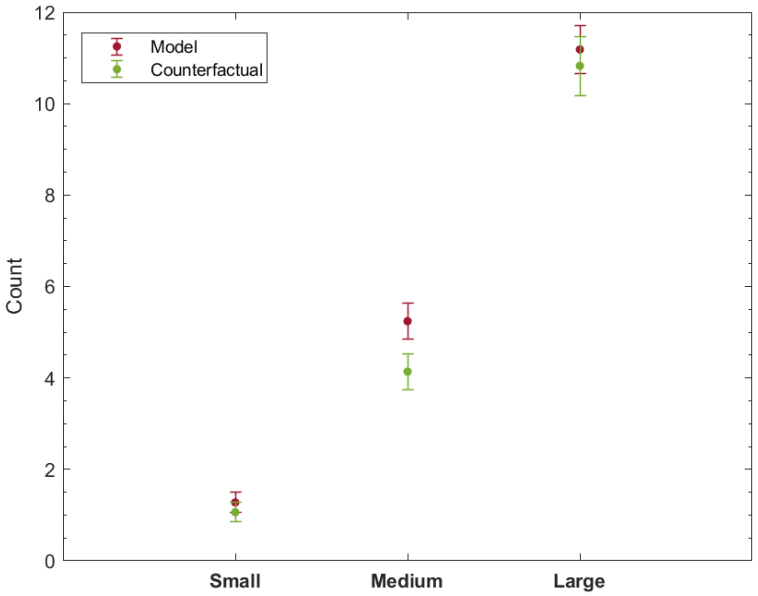
Notes: Dots are the point estimates for the number of acquired projects by phase, market size, and therapeutic category. The bars are the 95% confidence intervals. Model estimates based on 500 model simulations for 113 quarters, removing first 40 quarters.

Figure 13: Model Selection Across Phases



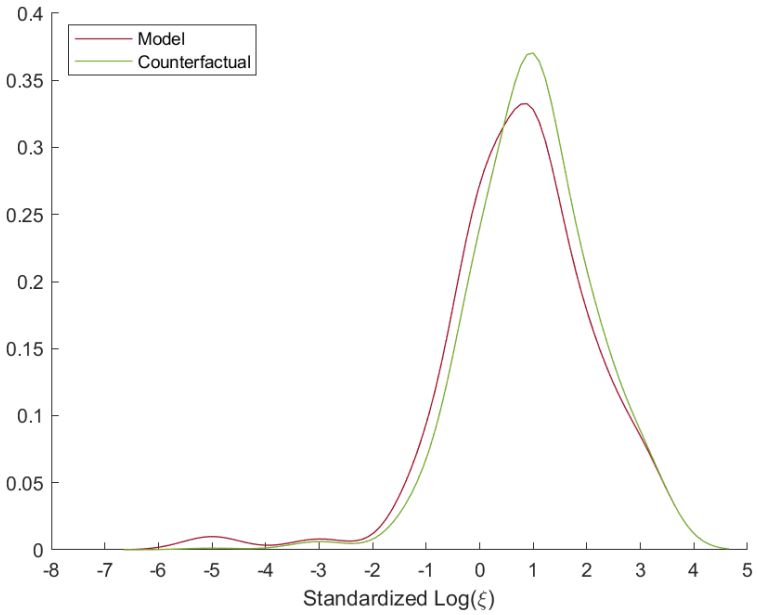
Notes: Simulated distribution of project quality by phase. *Top Left:* Startup, non-oncology markets. *Top Right:* Big firms, non-oncology markets. *Bottom Left*: Startups, oncology markets. *Bottom Right*: Big firms, oncology markets. Based on 500 model simulations for 113 quarters, removing first 40 quarters.

Figure 14: Counterfactual: Ban Startup Acquisitions - Approved Project Count



Notes: Dots are the point estimates for the count of total approved projects by market size and therapeutic category. The bars are the 95% confidence intervals. Based on 500 model simulations for 113 quarters, removing first 40 quarters. The counterfactual considers a ban on startup acquisitions where $\lambda_{a,x} = 0$ for all x. Only results from oncology markets are shown.

Figure 15: Counterfactual: Ban Startup Acquisitions - Distribution of Project Quality



Notes: Kernel density of log project quality standardized within market category for model and counterfactual. Based on 500 model simulations for 113 quarters, removing first 40 quarters. The counterfactual considers a ban on startup acquisitions where $\lambda_{a,x} = 0$ for all x. Only results from oncology markets are shown.

A Additional Descriptive Evidence

Table A1: Logit Phase Transition Coefficients - First-In-Class

	(1) Phase 0	(2) Phase I	(3) Phase II	(4) Phase III	(5) FDA
Acquired	-0.173	-0.761***	-0.0169	0.635**	0.710
	(0.106)	(0.135)	(0.151)	(0.281)	(0.550)
Big	0.755***	-0.257***	0.181***	0.313***	0.321*
	(0.0267)	(0.0435)	(0.0489)	(0.0965)	(0.178)
FIC	-0.459***	-0.345***	-0.530***	-0.287***	-0.210
	(0.0330)	(0.0533)	(0.0535)	(0.0972)	(0.173)
Biologic	0.233***	0.0551	0.122**	-0.127	0.239
	(0.0268)	(0.0466)	(0.0529)	(0.108)	(0.206)
LogCompPhase0	-1.206***	-0.520***	-0.0662	-0.244***	0.0234
	(0.0254)	(0.0434)	(0.0473)	(0.0844)	(0.154)
LogCompPhaseI	1.087***	-0.285***	-0.174***	-0.0143	0.000264
	(0.0367)	(0.0601)	(0.0637)	(0.116)	(0.209)
LogCompPhaseII	0.00143	0.752***	-0.883***	-0.376***	-0.576***
	(0.0284)	(0.0542)	(0.0595)	(0.107)	(0.211)
LogCompPhaseIII	0.186***	-0.00764	1.262***	-0.399***	0.00605
	(0.0273)	(0.0484)	(0.0617)	(0.103)	(0.191)
LogCompFDA	0.0735***	0.0397	0.109**	2.541***	0.299*
	(0.0235)	(0.0404)	(0.0464)	(0.113)	(0.160)
LogCompMkt	-0.252***	-0.258***	-0.181***	-0.271***	0.255*
	(0.0194)	(0.0338)	(0.0366)	(0.0709)	(0.151)
Constant	1.755***	2.783***	1.058***	1.061***	2.593***
	(0.0777)	(0.140)	(0.143)	(0.255)	(0.490)
Therap. Cat. FE	Y	Y	Y	Y	Y
N	34939	13840	8871	2723	1319
Pseudo-R^2	0.145	0.069	0.091	0.242	0.037

A project is first-in-class (FIC) if no other project with the same target-based action has been FDA approved. Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table A2: Logit Phase Transition Coefficients - Lead Projects

	(1) Phase 0	(2) Phase I	(3) Phase II	(4) Phase III	(5) FDA
Acquired	-0.0202	-0.718***	0.00929	0.757	12.92
	(0.114)	(0.149)	(0.208)	(0.533)	(413.8)
LeadAcquired	-1.075***	-0.237	-0.0701	-0.134	-12.52
	(0.316)	(0.336)	(0.293)	(0.612)	(413.8)
Big	0.763***	-0.245***	0.219***	0.352***	0.350**
	(0.0266)	(0.0434)	(0.0485)	(0.0954)	(0.176)
Biologic	0.209***	0.0288	0.0602	-0.166	0.212
	(0.0267)	(0.0463)	(0.0523)	(0.107)	(0.205)
LogCompPhase0	-1.216***	-0.522***	-0.0671	-0.246***	0.0151
	(0.0253)	(0.0433)	(0.0470)	(0.0844)	(0.155)
LogCompPhaseI	1.088***	-0.289***	-0.181***	-0.0181	0.00360
	(0.0366)	(0.0599)	(0.0633)	(0.116)	(0.209)
LogCompPhaseII	-0.00531	0.748***	-0.891***	-0.364***	-0.558***
	(0.0283)	(0.0541)	(0.0592)	(0.106)	(0.211)
LogCompPhaseIII	0.191***	-0.00691	1.258***	-0.410***	-0.0110
	(0.0272)	(0.0483)	(0.0614)	(0.103)	(0.190)
LogCompFDA	0.0805***	0.0485	0.123***	2.552***	0.308*
	(0.0235)	(0.0403)	(0.0461)	(0.113)	(0.160)
LogCompMkt	-0.240***	-0.249***	-0.166***	-0.259***	0.268*
	(0.0193)	(0.0337)	(0.0364)	(0.0707)	(0.150)
Constant	1.388***	2.510***	0.655***	0.806***	2.429***
	(0.0727)	(0.133)	(0.136)	(0.240)	(0.466)
Therap. Cat. FE	Y	Y	Y	Y	Y
N	34939	13840	8871	2723	1319
Pseudo-R^2	0.141	0.067	0.082	0.239	0.038

Lead projects defined as all projects in same stage of development as the acquired startup's highest phase project at the time of acquisition. Non-lead projects defined as all projects in earlier stages of development than the acquired startup's highest phase project at the time of acquisition. Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table A3: Startup Entry Event Study

	(1) OLS	(2) OLS	(3) Neg Bin	(4) Neg Bin
AcqWindow-5	0.669***	0.689***	0.285***	0.283***
	(0.0106)	(0.0102)	(0.00254)	(0.00305)
AcqWindow-4	1.057***	0.860***	0.298***	0.302***
	(0.131)	(0.118)	(0.0251)	(0.0249)
AcqWindow-3	1.112***	0.996***	0.336***	0.345***
	(0.133)	(0.125)	(0.0232)	(0.0252)
AcqWindow-2	1.146***	1.012***	0.323***	0.334***
	(0.152)	(0.136)	(0.0252)	(0.0254)
AcqWindow-1	1.178***	1.078***	0.347***	0.361***
	(0.148)	(0.136)	(0.0242)	(0.0254)
AcqWindow0	1.053***	0.885***	0.299***	0.313***
	(0.126)	(0.125)	(0.0279)	(0.0299)
AcqWindow1	0.824***	0.722***	0.253***	0.268***
	(0.0941)	(0.104)	(0.0234)	(0.0249)
AcqWindow2	1.051***	0.946***	0.317***	0.328***
	(0.110)	(0.114)	(0.0264)	(0.0269)
AcqWindow3	1.281***	1.148***	0.357***	0.366***
	(0.151)	(0.130)	(0.0233)	(0.0236)
AcqWindow4	0.841***	0.725***	0.260***	0.264***
	(0.171)	(0.154)	(0.0313)	(0.0306)
AcqWindow5	0.773***	0.773***	0.273***	0.291***
	(0.0595)	(0.0679)	(0.0101)	(0.0150)
Constant	0.296***	-0.691***	-0.727***	-0.633***
	(0.112)	(0.211)	(0.0875)	(0.114)
Mkt Size FE	Y	N	Y	N
Time FE	Y	N	Y	N
Mkt Size $\times$ Time FE	N	Y	N	Y
ICD-9 FE	Y	Y	Y	Y
N	14819	14819	14819	14819
Log Likelihood	-30551.5	-29805.3	-21301.5	-21214.6

The dependent variable y_{mt} is the count of startups that entered into market m at year-quarter t. Standard errors in parentheses are clustered at the ICD-9 level. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

B Big Firm Value Functions

The big firm's value function for $\phi \in \{1, 2, 3\}$ is given by:

$$
\begin{aligned}
&V(\xi_j, \phi_j, 2, n, x) = \\
&\left(\sum_{\phi=1}^{4} \lambda_{\phi,x} \cdot n_\phi + (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) + \rho \right)^{-1} \\
&\cdot \Bigg(-c_{\phi_j,2,y} + \sum_{\phi=1}^{3} \lambda_{\phi,x} (n_\phi - \mathbb{1}(\phi = \phi_j)) \cdot \Big(\hat{\sigma}_d(\phi, n, x) \cdot V(\xi_j, \phi_j, 2, n'(\phi, 1, 1), x) \\
&\qquad\qquad + (1 - \hat{\sigma}_d(\phi, n, x)) \cdot V(\xi_j, \phi_j, 2, n'(\phi, 1, 0), x) \Big) \\
&+ \lambda_4 \cdot n_4 \cdot V(\xi_j, \phi_j, 2, n'(4, 1, 0), x) \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) \cdot V(\xi_j, \phi_j, 1, n'(-1, 0, 1), x) \\
&+ \lambda_{\phi_j,x} \cdot \Big(\gamma + \log\big(1 + \exp\{\nu^{\mathbb{1}(\phi_j=3)} \cdot V(\xi_j, \phi_j + 1, 2, n'(\phi_j, 1, 1), x) - \mathbb{1}(\phi_j = 3) \cdot c_{FDA,2,y}\}\big) \Big) \Bigg)
\end{aligned}
\tag{20}
$$

Note that the big firm in clinical development cannot acquire nor be acquired. Further, an acquisition does not affect the moment the firm faces. The big firm's value function is only affected by an acquisition through the perceived transition probabilities.
The big firm's value function for $\phi = 4$ is given by:

$$
\begin{aligned}
&V(\xi_j, 4, 2, n, x) = \left(\sum_{\phi=1}^{4} \lambda_{\phi,x\phi} + (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) + \lambda_g + \rho \right)^{-1} \\
&\cdot \Bigg(\pi(\xi_j, 2, n_4, z) + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot (n_\phi - \mathbb{1}(\phi = \phi_j)) \cdot \Big(\hat{\sigma}_d(\phi, n, x) \cdot V(\xi_j, \phi_j, 2, n'(\phi, 1, 1), x) \\
&\qquad\qquad + (1 - \hat{\sigma}_d(\phi, n, x)) \cdot V(\xi_j, \phi_j, 2, n'(\phi, 1, 0), x) \Big) \\
&+ \lambda_4 \cdot (n_4 - 1) \cdot V(\xi_j, \phi_j, 2, n'(4, 1, 0), x) \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, n, x) \cdot V(\xi_j, \phi_j, 2, n'(-1, 0, 1), x) \Bigg)
\end{aligned}
\tag{21}
$$

C Sketch of Existence

Conditions for the existence of a MME are given in Appendix B of Ifrach and Weintraub (2016). Existence is proved using Brouwer's fixed point theorem. This requires showing:

1. The strategy space is convex and compact.
2. The equilibrium best response strategy function is continuous when competitors are play the equilibrium strategies.

D Computation

To compute the moment-based equilibrium strategies for the model described in Section 6, I follow Algorithm 1 of Ifrach and Weintraub (2016). This algorithm is based on the standard value function iteration algorithm used to solve for Markov perfect equilibrium policies, but with an added simulation step where the perceived transition probabilities are calculated. The algorithm begins with a guess of the value function $V(\hat{s})$ for all $\hat{s} \in \hat{S}$. Using the guess for the value function, we can compute the optimal strategies for all $\hat{s} \in \hat{S}$. We can then simulate a sample path using the optimal strategies and compute the perceived transition probabilities based on this sample path. The perceived transition probabilities together with the original guess for the value function imply a new guess for the value function at each moment-based state. The algorithm terminates when the equilibrium conditions have been sufficiently satisfied based on the norm of the distance between the original and new guess of the value function. The algorithm is repeated for each value of x, i.e. each market size and therapeutic category combination.

1. Begin with a guess $V^0(\hat{s})$ for all $\hat{s} \in \hat{S}$. Find the optimal strategies $\mathcal{A}^*$ implied by V^0 using equations (2), (3), (4), and (5).
2. Simulate a sample path over $t \in [0, \bar{T}]$ for large $\bar{T}$ using $\mathcal{A}^*$ to produce a dataset of observations $\{\hat{s}_l, t_l : l = 1, ..., T\}$, where $\hat{s}_l$ is the vector of firms' moment-based states immediately prior to the l-th non-continuation action in market t_l is the time the action is taken. Let j index the active firms so that $\hat{s}_{jl}$ is firm j's moment-based state. Compute the observed frequency of each moment and market-level state [42]:

$$h(n, x) = \sum_{l=1}^{T} \mathbb{1}(n_l = n, x), \ \forall n$$

[42] Note that the moment n_l and market-level state x_m is common to all firms' moment-based states at a given time t in a particular market m.

Compute the perceived transition probabilities:

$$\hat{\sigma}_{\mathcal{A}^*}(\phi, n, x) = \sum_{\theta=1}^{2} \sum_{\xi} \sigma_{\mathcal{A}^*}(\xi, \phi, \theta, n, x) \cdot \hat{P}_{\mathcal{A}^*}[\xi|\phi, \theta, n, x] \cdot \hat{P}_{\mathcal{A}^*}[\theta|\phi, n, x], \ \forall(\phi, n),$$

where

$$\hat{P}_{\mathcal{A}^*}[\xi|\phi, \theta, n, x] = \frac{\sum_l \sum_j \mathbb{1}(\xi_{jl} = \xi, \phi_{jl} = \phi, \theta_{jl} = \theta, n_l = n, x)}{\sum_l \sum_j \mathbb{1}(\phi_{jl} = \phi, \theta_{jl} = \theta, n_l = n, x)},$$

$$\hat{P}_{\mathcal{A}^*}[\theta|\phi, n, x] = \frac{\sum_l \sum_j \mathbb{1}(\theta_{jl} = \theta, \phi_{jl} = \phi, n_l = n, x)}{\sum_l n_{\phi l} \cdot \mathbb{1}(n_l = n, x)}.$$

3. Calculate $V^1(\hat{s})$ for all $\hat{s} \in \hat{S}$ using the perceived transition probabilities and V^0 in the right-hand side of equations (12) and (13). Find the new optimal strategies associated with V^1.

4. Calculate the norm: $max_{n_0} |\sum_{\hat{s}} (V^1(\hat{s}) - V^0(\hat{s})) \cdot \mathbb{1}(n = n_0, x)| \cdot h(n_0, x)$.

5. If the norm exceeds the acceptable threshold, update the guess of the value function with V_1 and the associated optimal strategies and repeat 2-5.

Note that for the moment-based states not in the recurrent class implied by the optimal strategies $\mathcal{A}^*$, the perceived transition probabilities are not defined. For these states, I assume that $\hat{P}_{\mathcal{A}^*}[\theta = 1|\phi, n, x] = 0$ and $\hat{P}_{\mathcal{A}^*}[\bar{\xi}|\phi, \theta, n, x] = 1$ for $\xi \in \{\underline{\xi}, ..., \bar{\xi}\}$. I am assuming that for a given phase, moment, and market state, the probability that a firm is a big firm is equal to one. I am also assuming that for a given phase, firm size, moment, and market state, the firm's quality is equal to the highest quality level with probability one. Beliefs about off-equilibrium-path behavior will still affect firms' strategies in the recurrent class. So different assumptions about the perceived transition probabilities outside of the recurrent class may have different implications for equilibrium outcomes.

E Binned Model

To keep the estimation and counterfactual simulations tractable, I use a grid to approximate the number of competitors in each phase. To see why this is necessary, consider a model with only one market size where the maximum number of competitors for each phase J_ϕ is equal to 15 and the discrete approximation to the Lognormal distribution for project quality contains seven points. This implies that there is $7 \times 4 \times 2 \times 16^3 \times 15 = 3,440,640$ possible states. Estimating this model using a nested fixed point algorithm and solving for the counterfactual is computationally challenging because the number of possible states grows exponentially in the number of state variables and the possible values that they can take. In the data, the largest market has a maximum number of competitors in each phase equal to (90, 130, 49, 58), making the use of a Markov Perfect Equilibrium impossible. Instead, using a grid of points to approximate the number of competitors in each phase can substantially reduce the size of the state space. The use of a moment-based equilibrium concept where the model is solved using simulation allows us to employ this approximation.

In the full model, the possible number of competitors for a particular phase ϕ and market size z is given by $n_\phi \in \{0, ..., J_{\phi,z}\}$. In the binned model, instead of counting each individual firm, we create a grid to partition the possible number of competitors and use the midpoint of each partition to approximate the number of competitors in each phase, which we denote by $\tilde{n}_\phi$. Let the total number of subsets in the partition equal $R+1$.[43] Let $\tilde{n}_\phi^r$ denote the midpoint of the subset $r \in \{1, ..., R+1\}$. Finally, denote the integer at the right edge of each partition by n_ϕ^r where $n_\phi^{R+1} = J_{\phi,z}$. Therefore, given the set $\{0, ..., J_{\phi,z}\}$, we create the partition

$$\{\{0, ..., n_\phi^1\}, \{n_\phi^1 + 1, ..., n_\phi^2\}, ..., \{n_\phi^R + 1, J_{\phi,z}\}\}.$$

Using the midpoint of each partition implies

$$\tilde{n}_\phi \in \left\{ \frac{n_\phi^1}{2}, \frac{n_\phi^2 + n_\phi^1 + 1}{2}, ..., \frac{J_{\phi,z} + n_\phi^R + 1}{2} \right\} \equiv \{\tilde{n}_\phi^1, \tilde{n}_\phi^2, ..., \tilde{n}_\phi^{R+1}\}.$$

The perceived transition probabilities now must take into account the probability that the moment $\tilde{n} = \{\tilde{n_1}, \tilde{n_2}, \tilde{n_3}, \tilde{n_4}\}$ changes conditional on a competitor taking a particular action. Where before a competing firm in phase ϕ choosing to advance to phase $\phi + 1$ would decrease n_ϕ by one and increase $n_{\phi+1}$ by one, now there is a discrete probability

[43] Though it is not the case here, the partition for each phase need not have the same number of subsets.

distribution that (i) $\tilde{n}_\phi$ and $\tilde{n}_{\phi+1}$ remain the same, (ii) $\tilde{n}_\phi$ decreases by one grid point and $\tilde{n}_{\phi+1}$ remains the same, (iii) $\tilde{n}_\phi$ remains the same and $\tilde{n}_{\phi+1}$ increases by one grid point, and (iv) $\tilde{n}_\phi$ decreases by one grid point and $\tilde{n}_{\phi+1}$ increases by one grid point. If a competing firm chooses not to advance to phase $\phi+1$, then only (i) and (ii) are possible.

The perceived transition probabilities must also account for the upper bounds on the total number of firms for each phase $J_{\phi,z}$. Because firms do not know the exact number of firms in each phase, they cannot know if a particular phase has hit its upper bound. To impose the upper bound, I modify the perceived transition probabilities to include an exogenous (to the focal firm) probability that the focal firm or a competitor is unable to move to the next phase even if they choose to do so when the state is equal to the highest grid point. The probability that the upper bound is binding when a competitor moves is directly incorporated into the perceived transition probability of moving to a different point on the grid of competitors conditional on a competitor's action (see equation (E1)). However, we must explicitly account for this probability when the focal firm moves.

Let $\tilde{s}_j = (\xi_j, \phi_j, \theta_j, \tilde{n}, x)$ denote the new moment-based state. Consider a dataset of observations $\{\tilde{s}_{ml}, t_{ml} : m = 1, ..., M, l = 1, ..., L_m\}$ sampled over the time interval $[0, \bar{T}]$ where $\tilde{s}_{ml}$ is the vector of firms' moment-based state immediately prior to the l-th non-continuation action in market m and t_{ml} is the time the action is taken. Let $\mathcal{A}_{jml} \in \{-1, 0, 1\}$ denote the action taken by firm j at move l for $\mathcal{A} \in \{a, d, e\}$. If firm j did not move at l, then $\mathcal{A}_{jml} = -1$. If firm j did move at l, but the move arrival was not for action $\mathcal{A}$, then $\mathcal{A}_{jml} = -1$. Index the grid points for phase ϕ by w and for phase $\phi+1$ by r. Define the probability that $\tilde{n}_\phi$ decreases by one grid point and $\tilde{n}_{\phi+1}$ increases by one grid point conditional on a competitor in phase ϕ choosing to advance to phase $\phi+1$ as follows

$$\hat{P}[\tilde{n}_{\phi+1}^{r+1}, \tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1] = \\ \underset{L\to\infty}{limsup} \frac{\sum_m \sum_l \sum_j \mathbb{1}(\phi_{jml} = \phi, \tilde{n}_{ml} = \tilde{n}, x_{ml} = x, d_{jml} = 1, \tilde{n}_{\phi+1,m,l+1} = \tilde{n}_{\phi+1}^{r+1}, \tilde{n}_{\phi,m,l+1} = \tilde{n}_\phi^{w-1})}{\sum_m \sum_l \sum_j \mathbb{1}(\phi_{jml} = \phi, \tilde{n}_{ml} = \tilde{n}, x_{ml} = x, d_j^{ml} = 1)}, \tag{E1}$$

where $\tilde{n}_{\phi+1,m,l} = \tilde{n}_{\phi+1}^r$ and $\tilde{n}_{\phi,m,l} = \tilde{n}_\phi^w$. Note that this implicitly accounts for the probability that the upper bound on the number of firms in phase $\phi+1$ is binding. Similarly, we can define $\hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1]$, $\hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1]$, and $\hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 0]$. Denote the probability that the upper bound on phase ϕ does not bind by

$$\hat{P}[n_\phi \neq J_{\phi,z} | \phi, \tilde{n}, x] = \underset{L\to\infty}{limsup} \frac{\sum_m \sum_l \mathbb{1}(n_{\phi ml} < J_{\phi,z}, \tilde{n}_{ml} = \tilde{n}, x_{ml} = x)}{\sum_m \sum_l \mathbb{1}(\tilde{n}_{ml} = \tilde{n}, x_{ml} = x)}. \tag{E2}$$

Define the function which describes changes in the moment $\tilde{n}$ as

$$\tilde{n}'(\phi, \tilde{\iota}_1, \tilde{\iota}_2) = \tilde{n} + \tilde{\iota_1} \cdot (\tilde{n}_\phi^{w-1} - \tilde{n}_\phi^w) \cdot \mathbb{e}_\phi + \tilde{\iota}_2 \cdot (\tilde{n}_{\phi+1}^{r+1} - \tilde{n}_{\phi+1}^r) \cdot \mathbb{e}_{\phi+1}.$$

where $\tilde{\iota}_1, \tilde{\iota}_2 \in \{0, 1\}$. The startup's value function for $\phi \in \{1, 2, 3\}$ becomes

$$
\begin{aligned}
&V(\xi_j, \phi_j, 1, \tilde{n}, x) = \\
&\Bigg(\lambda_{\phi_j,x} + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot \big(\tilde{n}_\phi - \mathbb{1}(\phi = \phi_j)\big) \cdot \Big[\hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \big(\hat{P}[\tilde{n}_{\phi+1}^{r+1}, \tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1] + \hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1] \\
&+ \hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1]\big) + \big(1 - \hat{\sigma}_d(\phi, \tilde{n}, x)\big) \cdot \hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 0]\Big] + \lambda_4 \cdot \tilde{n}_4 \cdot \hat{P}[\tilde{n}_4^{w-1} | 4, \tilde{n}, x] \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_0^{r+1} | 0, \tilde{n}, x, e = 1] \\
&+ \lambda_{a,x} \cdot (\Sigma_{\phi=1}^3 \tilde{n}_\phi \cdot \hat{P}[\theta = 1 | \phi, \tilde{n}, x])^{-1} \cdot \sigma_a(\xi_j, \phi_j, 1, \tilde{n}, x) \cdot (1 - \kappa) + \rho\Bigg)^{-1} \\
&\cdot \Bigg(-c_{\phi_j,1,y} + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot (\tilde{n}_\phi - \mathbb{1}(\phi = \phi_j)) \cdot \Big[\hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_{\phi+1}^{r+1}, \tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(\phi, 1, 1), x) \\
&+ \hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(\phi, 0, 1), x) \\
&+ \big(\hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1] + (1 - \hat{\sigma}_d(\phi, \tilde{n}, x)) \cdot \hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 0]\big) \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(\phi, 1, 0), x)\Big] \\
&+ \lambda_4 \cdot \tilde{n}_4 \cdot \hat{P}[\tilde{n}_4^{w-1} | 4, \tilde{n}, x] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(4, 1, 0), x) \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_0^{r+1} | 0, \tilde{n}, x, e = 1] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(-1, 0, 1), x) \\
&+ \lambda_{a,x} \cdot (\Sigma_{\phi=1}^3 \tilde{n}_\phi \cdot \hat{P}[\theta = 1 | \phi, \tilde{n}, x])^{-1} \cdot \sigma_a(\xi_j, \phi_j, 1, \tilde{n}, x) \cdot (1 - \kappa) \cdot V(\xi_j, \phi_j, 2, \tilde{n}, x) \\
&+ \lambda_{\phi_j,x} \cdot \Big[\gamma + \log\big(1 + \exp\big\{\nu^{\mathbb{1}(\phi_j = 3)} \cdot \hat{P}[n_\phi \neq J_{\phi,z} | \phi, \tilde{n}, x] \cdot \big[\hat{P}[\tilde{n}_{\phi_j+1}^{r+1}, \tilde{n}_{\phi_j}^{w-1} | \phi_j, \tilde{n}, x, d_j = 1, n_\phi \neq J_{\phi,z}] \\
&\cdot V(\xi_j, \phi_j + 1, 1, \tilde{n}'(\phi_j, 1, 1), x) + \hat{P}[\tilde{n}_{\phi_j+1}^{r+1} | \phi_j, \tilde{n}, x, d_j = 1, n_\phi \neq J_{\phi,z}] \cdot V(\xi_j, \phi_j + 1, 1, \tilde{n}'(\phi_j, 0, 1), x) \\
&+ \hat{P}[\tilde{n}_{\phi_j}^{w-1} | \phi_j, \tilde{n}, x, d_j = 1, n_\phi \neq J_{\phi,z}] \cdot V(\xi_j, \phi_j + 1, 1, \tilde{n}'(\phi_j, 1, 0), x) \\
&+ \hat{P}[\tilde{n} | \phi_j, \tilde{n}, x, d_j = 1, n_\phi \neq J_{\phi,z}] \cdot V(\xi_j, \phi_j + 1, 1, \tilde{n}'(\phi_j, 0, 0), x)\big] - \mathbb{1}(\phi_j = 3) \cdot c_{FDA,1,y}\big\}\big)\Big]\Bigg)
\end{aligned}
$$

The startup's value function for $\phi = 4$ is given by

$$
\begin{aligned}
&V(\xi_j, \phi_j, 1, \tilde{n}, x) = \\
&\Bigg(\lambda_{4,x} + \lambda_g + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot \tilde{n}_\phi \cdot \Big[\hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \big(\hat{P}[\tilde{n}_{\phi+1}^{r+1}, \tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1] + \hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1] \\
&+ \hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1]\big) + \big(1 - \hat{\sigma}_d(\phi, \tilde{n}, x)\big) \cdot \hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 0]\Big] + \lambda_4 \cdot (\tilde{n}_4 - 1) \cdot \hat{P}[\tilde{n}_4^{w-1} | 4, \tilde{n}, x] \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_0^{r+1} | 0, \tilde{n}, x, e = 1] + \rho\Bigg)^{-1} \\
&\cdot \Bigg(\pi(\xi_j, 1, \tilde{n}_4, z) + \sum_{\phi=1}^{3} \lambda_{\phi,x} \cdot \tilde{n}_\phi \cdot \Big[\hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_{\phi+1}^{r+1}, \tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 1] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(\phi, 1, 1), x) \\
&+ \hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(\phi, 0, 1), x) \\
&+ \big(\hat{\sigma}_d(\phi, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_{\phi+1}^{r+1} | \phi, \tilde{n}, x, d = 1] + (1 - \hat{\sigma}_d(\phi, \tilde{n}, x)) \cdot \hat{P}[\tilde{n}_\phi^{w-1} | \phi, \tilde{n}, x, d = 0]\big) \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(\phi, 1, 0), x)\Big] \\
&+ \lambda_4 \cdot (\tilde{n}_4 - 1) \cdot \hat{P}[\tilde{n}_4^{w-1} | 4, \tilde{n}, x] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(4, 1, 0), x) \\
&+ (\lambda_{e,1,x} + \lambda_{e,2,x}) \cdot \hat{\sigma}_e(-1, \tilde{n}, x) \cdot \hat{P}[\tilde{n}_0^{r+1} | 0, \tilde{n}, x, e = 1] \cdot V(\xi_j, \phi_j, 1, \tilde{n}'(-1, 0, 1), x)\Bigg)
\end{aligned}
$$

The solution method for this model is analogous to that described in Appendix D. For moment-based states that are outside of the recurrent class, I assume that the moment $\tilde{n}$ remains the same: $\hat{P}[\tilde{n} | \phi, \tilde{n}, x, d = 1] = 1$, $\hat{P}[\tilde{n} | \phi, \tilde{n}, x, d = 0] = 1$, and $\hat{P}[\tilde{n} | 4, \tilde{n}, x] = 1$. I also assume that the upper bound never binds: $\hat{P}[n_\phi \neq J_{\phi,z} | \phi, \tilde{n}, x] = 1$. The estimation of this model is virtually the same except that now the conditional choice probabilities, value function, and perceived choice probabilities depend on $\tilde{n}$ instead of n. The perceived transition probabilities between moments $\tilde{n}$ and the probability that the upper bound is binding are estimated using the frequency estimators as in equations (E1) and (E2), respectively.

F First Stage Estimates

Table F1: Rate Parameter Estimates

Market	Parameter							
(y, z)	$\lambda_{e,1,x}$	$\lambda_{e,2,x}$	$\lambda_{1,x}$	$\lambda_{2,x}$	$\lambda_{3,x}$	λ_4	λ_g	$\lambda_{a,x}$
Small, Other	0.4477	0.1695	0.1021	0.05108	0.0369	0.0010	0.0200†	0.0324†
$(1, 1)$	(0.0090)	(0.0055)	(0.0024)	(0.0015)	(0.0017)	(0.0001)		
Small, Onc.	0.3932	0.1919	0.1011	0.0337	0.0369	0.0010	0.0200†	0.1074†
$(1, 2)$	(0.0184)	(0.0128)	(0.0046)	(0.0020)	(0.0051)	(0.0001)		
Med., Other	1.4116	0.5892	0.0958	0.0493	0.0380	0.0010	0.0200†	0.0684†
$(2, 1)$	(0.0181)	(0.0117)	(0.0017)	(0.0011)	(0.0014)	(0.0001)		
Med., Onc.	1.4131	0.6118	0.0927	0.0392	0.0373	0.0010	0.0200†	0.2542†
$(2, 2)$	(0.0420)	(0.0276)	(0.0029)	(0.0015)	(0.0032)	(0.0001)		
Large, Other	5.2609	2.3517	0.0833	0.0491	0.0400	0.0010	0.0200†	0.2961†
$(3, 1)$	(0.0490)	(0.0328)	(0.0012)	(0.0009)	(0.0013)	(0.0001)		
Large, Onc.	3.5627	1.3446	0.0892	0.0389	0.0319	0.0010	0.0200†	0.6206†
$(3, 2)$	(0.0666)	(0.0408)	(0.0018)	(0.0009)	(0.0018)	(0.0001)		

†Externally calibrated parameter. $\lambda_{a,x}$ is set equal to three times the observed acquisition rate. Durations are equal to $1/\lambda$. The reference unit time period is a quarter. Standard errors are in parentheses.

Table F2: Choice Probability Regression - Small Markets

	(1) Entry	(2) Phase I	(3) Phase II	(4) Phase III
CompPhaseI	0.00182	0.0106	-0.0252	0.0218
	(0.0126)	(0.0188)	(0.0229)	(0.0391)
CompPhaseII	0.0110	0.0144	-0.0447***	-0.0288
	(0.00884)	(0.0151)	(0.0118)	(0.0241)
CompPhaseIII	0.0289	-0.0483	-0.0200	0.00954
	(0.0187)	(0.0297)	(0.0289)	(0.0348)
CompMkt	-0.0287***	-0.0436**	0.0101	-0.0336
	(0.0108)	(0.0171)	(0.0165)	(0.0224)
Oncology	0.997***	0.679***	-0.745***	-0.152
	(0.103)	(0.190)	(0.162)	(0.324)
Constant	0.0209	1.740***	0.377**	0.524*
	(0.0960)	(0.163)	(0.159)	(0.273)
N	4105	2229	1498	542
Pseudo-R^2	0.026	0.022	0.033	0.006

Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table F3: Choice Probability Regression - Medium Markets

	(1) Entry	(2) Phase I	(3) Phase II	(4) Phase III
CompPhaseI	0.0165*	0.0247	-0.00609	-0.0613**
	(0.00909)	(0.0168)	(0.0178)	(0.0307)
CompPhaseI^2	-0.000470*	-0.00132***	0.0000413	0.00205**
	(0.000266)	(0.000465)	(0.000512)	(0.000904)
CompPhaseII	0.0218***	0.000179	-0.0599***	-0.0526**
	(0.00693)	(0.0126)	(0.0134)	(0.0233)
CompPhaseII^2	-0.000333**	0.000434	0.000911***	0.000837*
	(0.000150)	(0.000265)	(0.000275)	(0.000504)
CompPhaseIII	0.0926***	0.0122	0.0778**	0.0734
	(0.0190)	(0.0327)	(0.0363)	(0.0565)
CompPhaseIII^2	-0.00351***	-0.00163	-0.00452*	-0.00674**
	(0.00121)	(0.00202)	(0.00234)	(0.00332)
CompMkt	-0.0419**	-0.0845***	-0.0452	0.123**
	(0.0180)	(0.0326)	(0.0346)	(0.0588)
CompMkt^2	0.00167*	0.00334**	0.00275	-0.00345
	(0.000950)	(0.00168)	(0.00179)	(0.00298)
Oncology	1.180***	0.381***	-0.420***	0.0975
	(0.0702)	(0.123)	(0.129)	(0.273)
Constant	-0.948***	1.328***	0.176	-0.0195
	(0.0862)	(0.170)	(0.181)	(0.312)
N	10237	4237	2719	878
Pseudo-R^2	0.048	0.024	0.025	0.033

Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table F4: Choice Probability Regression - Large Markets

	(1) Entry	(2) Phase I	(3) Phase II	(4) Phase III
CompPhaseI	-0.0202***	-0.0490***	-0.0161	0.0328
	(0.00482)	(0.00981)	(0.0107)	(0.0201)
CompPhaseI^2	0.000126**	0.000379***	0.000173	-0.000424*
	(0.0000549)	(0.000109)	(0.000120)	(0.000227)
CompPhaseII	0.0332***	0.0271***	-0.0275***	-0.0202
	(0.00301)	(0.00548)	(0.00712)	(0.0126)
CompPhaseII^2	-0.000260***	-0.000209***	0.000159***	0.000120
	(0.0000244)	(0.0000439)	(0.0000561)	(0.000100)
CompPhaseIII	0.0249***	0.0183	0.0196	0.0828***
	(0.00752)	(0.0137)	(0.0163)	(0.0313)
CompPhaseIII^2	-0.000376**	-0.000193	-0.000136	-0.00183***
	(0.000172)	(0.000310)	(0.000368)	(0.000687)
CompMkt	0.0105**	0.0199**	0.00689	0.0577***
	(0.00510)	(0.00913)	(0.0106)	(0.0193)
CompMkt^2	-0.000595***	-0.000739***	-0.00000131	-0.000846**
	(0.000109)	(0.000192)	(0.000224)	(0.000391)
Oncology	1.413***	1.042***	-0.143	-0.517***
	(0.0467)	(0.0794)	(0.0895)	(0.174)
Constant	-1.172***	1.017***	0.0421	-1.111***
	(0.0810)	(0.169)	(0.179)	(0.352)
N	20599	7374	4654	1276
Pseudo-R^2	0.082	0.052	0.019	0.046

Dependent variable *ReachPhasek+1* is equal to one if a project successfully passes the development phase k, zero otherwise. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table F5: Firm Type Regression - Small Markets

	(1) Phase I	(2) Phase II	(3) Phase III
CompPhaseI	-0.0222***	-0.00917***	0.00661
	(0.00293)	(0.00271)	(0.00505)
CompPhaseII	-0.00256	-0.00233	0.0119***
	(0.00237)	(0.00173)	(0.00339)
CompPhaseIII	0.0172***	0.0184***	0.00597
	(0.00625)	(0.00539)	(0.00570)
CompMkt	-0.00794**	-0.0138***	0.00580
	(0.00401)	(0.00343)	(0.00380)
Oncology	-0.166***	-0.277***	-0.170***
	(0.0308)	(0.0242)	(0.0510)
Constant	0.678***	0.580***	-0.247***
	(0.0332)	(0.0284)	(0.0428)
N	30170	44803	17457
Pseudo-R^2	0.003	0.004	0.001

Dependent variable is equal to one if an active firm is a startup. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table F6: Firm Type Regression - Medium Markets

	(1) Phase I	(2) Phase II	(3) Phase III
CompPhaseI	0.0118***	0.00592***	-0.00829**
	(0.00280)	(0.00222)	(0.00346)
CompPhaseI^2	-0.000742***	-0.000219***	-0.000119
	(0.0000713)	(0.0000581)	(0.0000934)
CompPhaseII	-0.0134***	-0.00983***	-0.00503*
	(0.00194)	(0.00182)	(0.00265)
CompPhaseII^2	0.000390***	0.000280***	0.000472***
	(0.0000374)	(0.0000340)	(0.0000528)
CompPhaseIII	-0.0819***	-0.0714***	-0.0775***
	(0.00448)	(0.00381)	(0.00601)
CompPhaseIII^2	0.00482***	0.00377***	0.00342***
	(0.000271)	(0.000226)	(0.000322)
CompMkt	-0.0538***	-0.0309***	0.0500***
	(0.00458)	(0.00390)	(0.00651)
CompMkt^2	0.00259***	0.00160***	-0.00208***
	(0.000237)	(0.000203)	(0.000330)
Oncology	0.0210	0.0512***	0.220***
	(0.0153)	(0.0129)	(0.0250)
Constant	0.971***	0.735***	0.0445
	(0.0290)	(0.0252)	(0.0382)
N	149712	201338	71815
Pseudo-R^2	0.008	0.003	0.014

Dependent variable is equal to one if an active firm is a startup. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

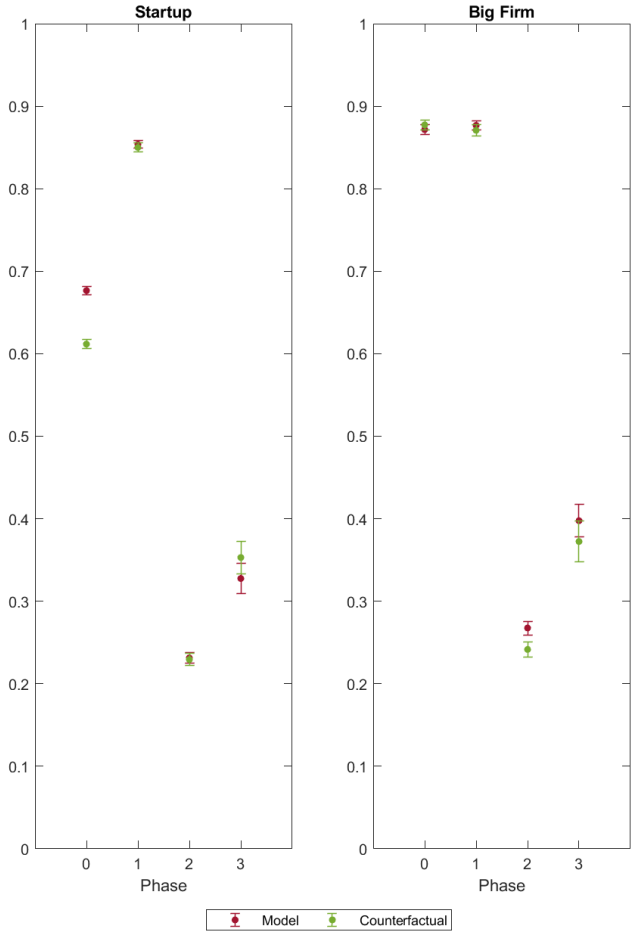
Table F7: Firm Type Regression - Large Markets

	(1) Phase I	(2) Phase II	(3) Phase III
CompPhaseI	0.00661***	0.00407***	0.0267***
	(0.00118)	(0.00106)	(0.00169)
CompPhaseI^2	-0.000100***	-0.0000563***	-0.000277***
	(0.0000128)	(0.0000114)	(0.0000183)
CompPhaseII	-0.00638***	-0.00466***	-0.000986
	(0.000584)	(0.000645)	(0.000975)
CompPhaseII^2	0.0000209***	0.0000205***	-0.0000341***
	(0.00000450)	(0.00000490)	(0.00000749)
CompPhaseIII	0.0144***	0.0146***	-0.00436*
	(0.00133)	(0.00122)	(0.00230)
CompPhaseIII^2	-0.000115***	-0.000189***	0.000396***
	(0.0000293)	(0.0000268)	(0.0000492)
CompMkt	-0.00723***	-0.00544***	-0.0246***
	(0.000800)	(0.000709)	(0.00127)
CompMkt^2	0.000102***	0.000126***	0.000190***
	(0.0000163)	(0.0000147)	(0.0000251)
Oncology	0.261***	0.249***	0.252***
	(0.00624)	(0.00551)	(0.00984)
Constant	0.465***	0.343***	-0.351***
	(0.0216)	(0.0189)	(0.0307)
N	778394	972639	305783
Pseudo-R^2	0.004	0.003	0.013

Dependent variable is equal to one if an active firm is a startup. Logit regression coefficients are shown. Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

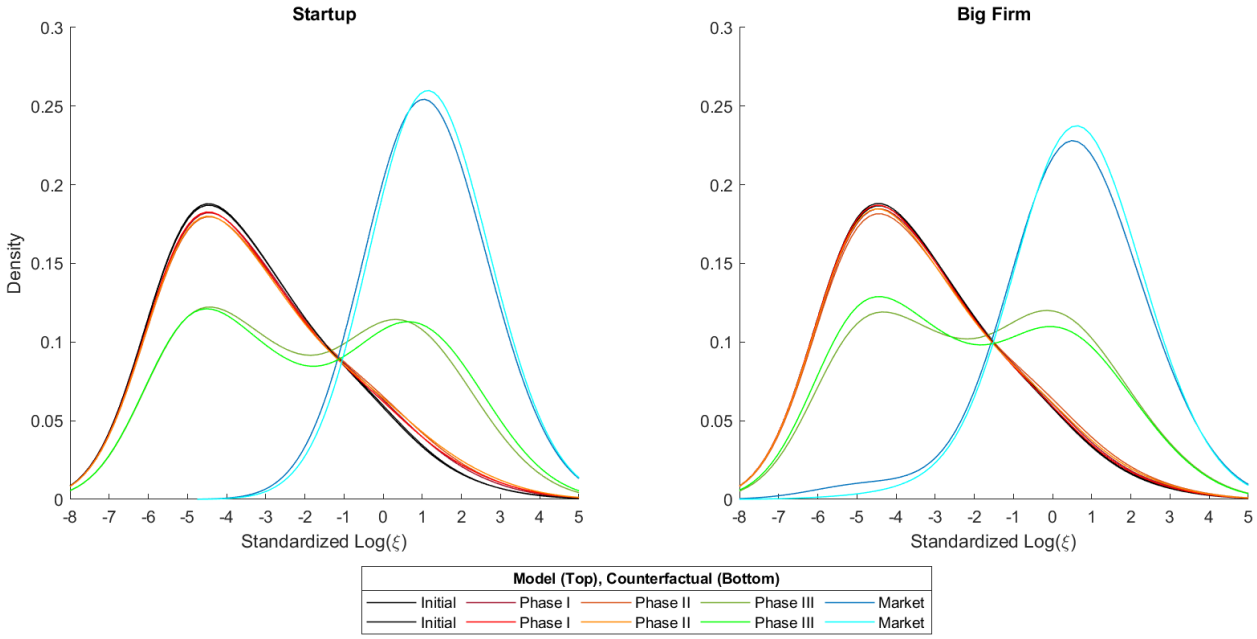
G Additional Counterfactual Figures

Figure G1: Counterfactual: Ban Startup Acquisitions - Transition Probabilities



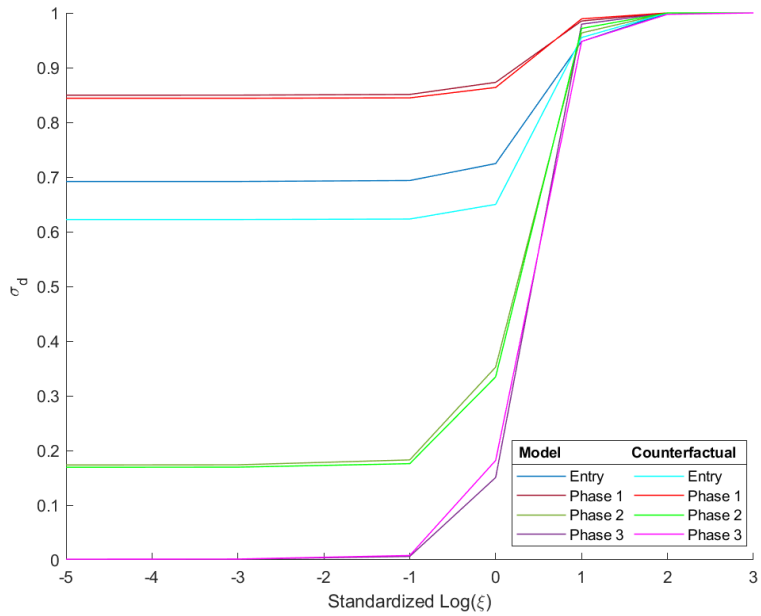
Notes: Dots are the point estimates for the transition probabilities by phase, firm type, therapeutic category. The bars are the 95% confidence intervals. Based on 500 model simulations for 113 quarters, removing first 40 quarters. The counterfactual considers a ban on startup acquisitions where $\lambda_{a,x} = 0$ for all x. Only results from oncology markets are shown.

Figure G2: Counterfactual: Ban Startup Acquisitions - Selection Across Phases



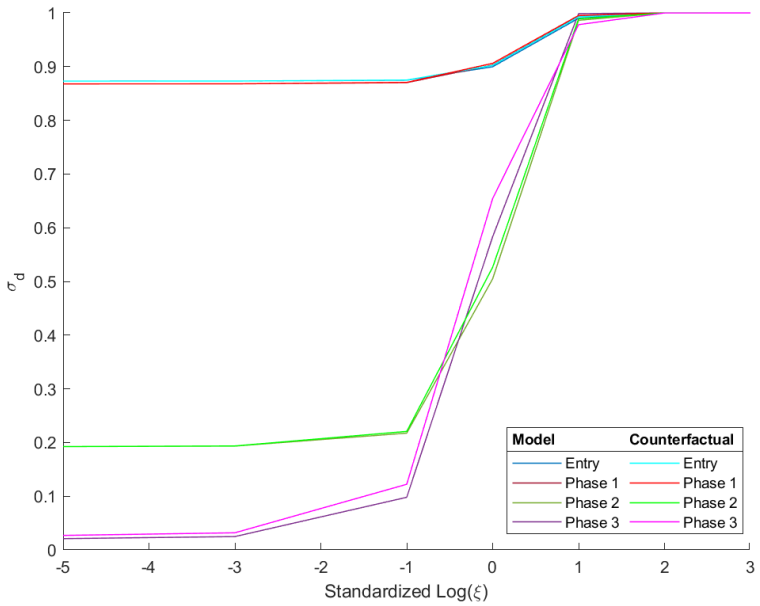
Notes: Model and counterfactual distribution of project quality by phase. Based on 500 model simulations for 113 quarters, removing first 40 quarters. The counterfactual considers a ban on startup acquisitions where $\lambda_{a,x} = 0$ for all x. Only results from oncology markets are shown.

Figure G3: Counterfactual: Ban Startup Acquisitions - Startup Development Policy Functions



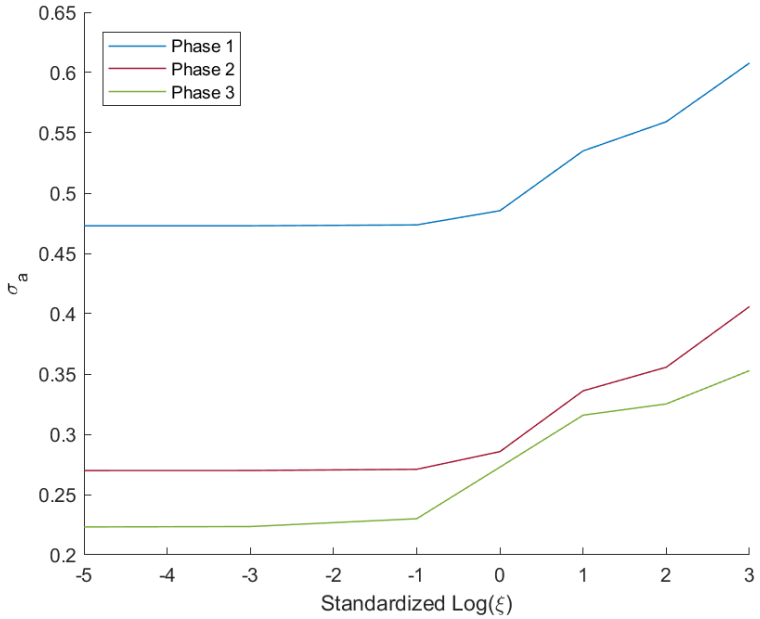
Notes: Development policy functions weighted by frequency of the moment and market-level state in equilibrium. The counterfactual considers a ban on startup acquisitions where $\lambda_{a,x} = 0$ for all x. Only results from oncology markets are shown.

Figure G4: Counterfactual: Ban Startup Acquisitions - Big Firm Development Policy Functions



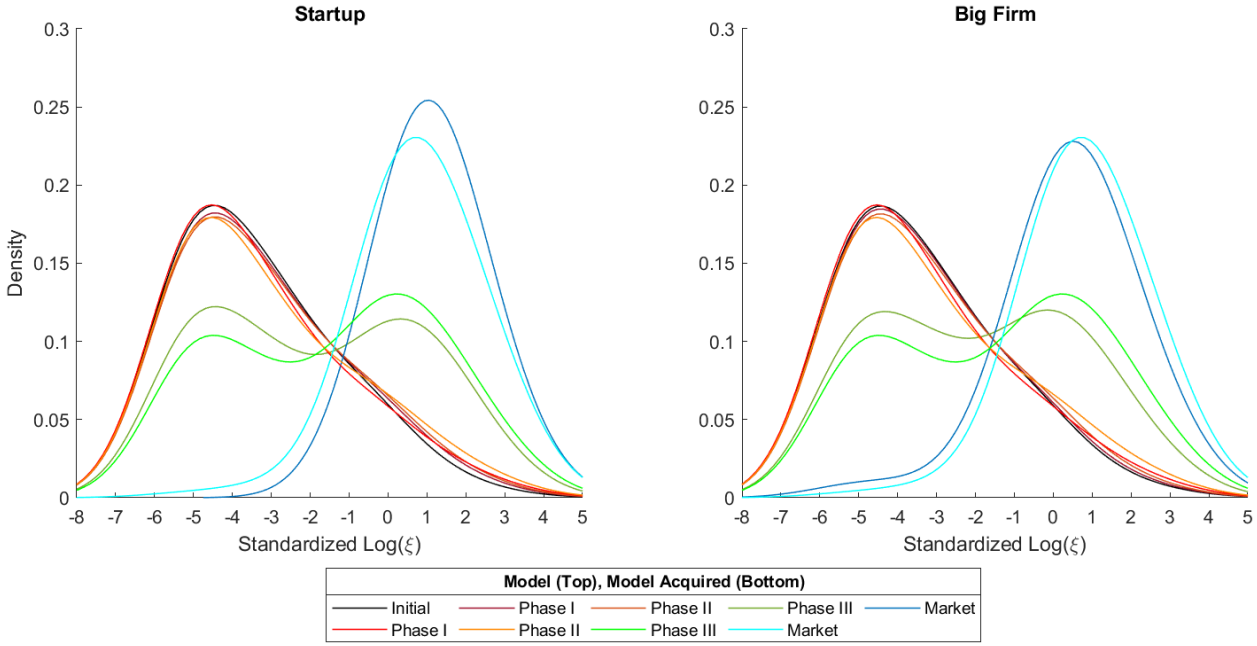
Notes: Development policy functions weighted by frequency of the moment and market-level state in equilibrium. Counterfactual 1 considers a ban on startup acquisitions where $\lambda_{a,x} = 0$ for all x. Only results from oncology markets are shown.

Figure G5: Acquisition Policy Functions



Notes: Acquisition policy functions weighted by frequency of the moment and market-level state in equilibrium. Only results from oncology markets are shown.

Figure G6: Model Selection Across Phases - Acquired vs. All



Notes: Model distribution of project quality by phase and acquisition status (all projects vs. acquired projects). Based on 500 model simulations for 113 quarters, removing first 40 quarters. Only results from oncology markets are shown.