Dusting Off the Old Ones: Drug Licensing to Startups, Innovation Success and Efficiency *

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Abstract

This paper investigates whether startups bring efficiency to product innovation relative to larger firms. Using comprehensive drug development data, we examine the innovation of drug projects licensed from large firms to startups. We find that these licensed projects are more likely to be developed and approved relative to comparable projects originated by larger firms but never licensed, or licensed between large firms. Relative to the other (never-licensed) projects in the licensor's portfolio, out-licensed projects are older, more likely to use new technology, and target a new market with longer development times and lower revenues. We also find that startups are more likely to in-license projects that target existing markets but use new technology. Our findings underscore the importance of entrepreneurial firms in complementing the 'shelved' innovation of large firms and improving their efficiency.

Keywords: Firm Boundary, Startups, Conglomerates, Product Innovation, Research and Development, Drug Licensing, Product Market

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1 Introduction

Can entrepreneurial firms bring efficiency to innovation with the presence of conglomerates? Would it be socially optimal to spin off or license some research and development (R&D) projects from large companies to startups to speed up the process of bringing ideas to product markets? The answers to the above questions are unclear. On the one hand, startups face financial constraints in research and development, while large companies have a more developed internal capital market as well as internal labor market (Maksimovic & Phillips, 2013; Stein, 1997). On the other hand, there are concerns over large companies regarding resource misallocation and empire-building of managers, which may lead to inefficiency in innovation (Gormley & Matsa, 2011; Rajan, Servaes, & Zingales, 2000). One particular concern is that conglomerates may "shelve" certain projects that are still under development before the innovation is realized and introduced to the market for various reasons. For example, conglomerates might need to prioritize other projects in the portfolio due to external pressures or economic considerations like the competitiveness of the product market and the overlap with existing products.[1]

The empirical literature investigating the effects of innovation shelving is scarce. In particular, hardly any work has been done to investigate whether startups see an opportunity to complete the development of these abandoned projects, despite their economic importance. There are several reasons why these topics are under-researched. Most importantly is the difficulty in observing shelved innovation, since information on firm innovation is aggregated to the firm level in most industries, which means that detailed innovation data is rarely available. This poses a challenge in identifying shelved projects and the subsequent licensing of said projects by startups. The second

[1]For example, an article published on techcrunch.com highlights this issue stating that big pharma companies often abandon the development of promising drugs for reasons "having nothing to do with their efficacy. Sometimes it's a strategic decision to focus elsewhere."

reason is due to the difficulty of identifying clear milestones in R&D, which is necessary for determining the success and efficiency of the innovation process.[2] Third, studying these (under-researched) topics requires an empirical setting where changes in R&D project ownership are common. That is, frequent transfer in the ownership, or licensing, of intellectual property. Finally, the need to focus on product markets that include both large and mature innovators, with multiple projects, and smaller more focused newcomers.

The pharmaceutical sector is well suited to address the challenges stated above. Specifically, we use drug development data to study whether licensing from "big to small" could improve innovation efficiency for several reasons. First, the project-level development data enable us to overcome the challenge of observing whether a project has been shelved by a large company. The data also provides information on the licensing of a project as well as the innovation outcome, allowing us to track a project's milestones before and after the licensing event. Second, both large pharmaceutical companies and startups are active innovators in the pharmaceutical industry. For example, the successful development of Covid-19 vaccine involved both large pharmaceutical companies like Pfizer and entrepreneurial firms such as Moderna and BioNTech. Furthermore, individual drug acquisitions and licensing between conglomerates and startups are commonplace and frequent in the pharmaceutical sector (Cunningham, Ederer, & Ma, 2021; Hermosilla, 2021; Thakor et al., 2017). Third, drug development itself is critical for societal welfare but faces several difficulties, including large costs of R&D, long investment horizon, and a high risk of failure, which may lead to the

[2]We argue that patents should not be viewed as milestones because it often takes several years from the patent grant date to product introduction. For example, in the biopharmaceutical industry, approved drugs usually have about 5 years of patent coverage remaining (patents coverage normally lasts 20 years from the patent grant date). Furthermore, the granting of a patent does not guarantee that the granted product will be introduced to the market. For example, in our Cortellis drug development data, only about 43% of patented projects are eventually approved-for-sale.

"shelving" of a drug project.[3] Finally, the sector has recently witnessed an emerging trend of startup drug project in-licensing from large firms.[4]

Why do large firms shelve and subsequently out-license potentially promising projects to startups? What are the characteristics of these projects relative to the other projects owned by the same licensor? We are unable to answer the first question conclusively since firms may choose to shelf or out-license a project for many reasons. Moreover, firms are often reluctant to share details on the abandonment of a project (see for example, Krieger 2021). However, our comprehensive drug development data enables us to adequately answer the second question. We construct cross-sectional data that includes all projects owned by the licensor in quarters when a startup licensing event had occurred. We examine the characteristics of the out-licensed project relative to the same licensor's other projects. We find that out-licensed projects are significantly older than the other (non-licensed) projects, which is consistent with them being abandoned (shelved). Furthermore, we find that out-licensed projects are more likely to use a new technology that wasn't used previously in any of the licensor's other projects, and they're also more likely to target a new market with more approved products, longer clinical development times, and lower reported sales. These findings suggest that large and established licensors are more likely to let go of projects (by licensing them off to startups) if: (i) they have been sitting on the shelf for a long time, (ii) the licensor has no prior experience developing projects with their technology or targeting

[3]The cost of R&D is $4 to $8 million for Phase I trial, and $13 to $80 million for phase II trials (Adams & Brantner, 2006; Sertkaya, Birkenbach, Berlind, & Eyraud, 2014). The average time from drug discovery to FDA approval is 5 to 8 years (Garfinkel & Hammoudeh, 2020). On average, only 10% of projects entered Phase I, 16% of Phase II, and 50% of Phase III can receive an FDA approval (Hay, Thomas, Craighead, Economides, & Rosenthal, 2014).

[4]One example is the licensing of antibiotic SPR994 from Meiji Seika, a large Japanese pharmaceutical company, to the startup company, Spero, in 2017 with the goal specifically being to "tee up a Phase I study of SPR994 and then move straight into a pivotal Phase III for community-acquired urinary tract infections."2 Spero raised $51.7 million in the round of financing before the in-licensing event and its main venture capital investors including Atlas, SR One, and Google Ventures. Source: https://endpts.com/shooting-for-phiii-spero-tees-up-a-new-lead-antibiotic-in-licensed-cheap-as-it-lines-up-86m-ipo/.

their market, (iii) if the development time is lengthy, and (iv) if their targeted market generates fewer revenues. We next rerun the same analysis as above only focusing on the portfolio of the startup licensee. We construct similar cross-sectional data and investigate the characteristics of the in-licensed projects relative to the other ones owned by the same startup licensee. We find that in-licensed projects are more likely to have a new technology never used before in any of the licensee's other projects. Moreover, we find that the exposure (calculated as the number of firm projects in a market divided by total firm projects) of a licensee's drug portfolio to a project's market is strongly associated with an in-licensing event. The findings suggest that startups seek to license projects that target familiar markets only using new technology.

We subject our findings to a battery of robustness tests. First, we show that our results are not driven by systematic differences between the treatment and control groups in the baseline sample. We create an alternative sample with more comparable treatment and control projects. For each treatment project, we randomly select a project from a pool of all potential control projects that (i) target the same market, (ii) with the same stage of development, (iii) drug age, and (iv) are developed by firms with similar size. We further require that these drug projects (v) must have never experienced any licensing events, i.e., they are owned and developed by a single. Consistent with our baseline sample findings, we find that big-to-small projects are more likely to be developed and approved. Second, we show that our results are not driven by our choice for the regression model. We successfully replicate our results using alternative regression models including Logit, Conditional (Fixed Effects) Logit, and the Cox proportional-hazards regressions.

The rest of the paper is organized as follows. Section 2 discusses the contribution of this study to related literature. Section 3 introduces the institutional background of drug development and licensing. Section 4 describes the data sources and the con-

struction of the sample and variables. Section 5 shows the empirical strategy and main results of how the licensing from large companies to small companies might add efficiency and increase the likelihood of successes in the drug development process. Section 6 concludes the paper.

2 Related Literature and Contribution

The main contribution of our paper is to document how entrepreneurial firms may facilitate innovation efficiency and success by licensing projects from large companies. Previous literature has shown that conglomerates with multiple divisions have both upside and downside allocating resources in the internal capital market and labor market (Hart, 1995; Rajan et al., 2000; Stein, 1997). The empirical evidence so far is mixed when looking at different aspects of firm performances. Starting with examining the valuation of firms, Lang and Stulz (1994) and Berger and Ofek (1995) document that diversified firms trade at a discount compared with standalone firms while Graham, Lemmon, and Wolf (2002) and Campa and Kedia (2002) suggest that the discount is not evidence for inefficiency. Schoar (2002) proposes a positive "new toy" effect in productivity for the new segments in diversified firms but a negative effect in productivity for the whole conglomerates. Seru (2014) shows that target firms acquired by conglomerates produce less quantity and quality of patents. However, there has been little research directly showing the evidence of "shelfing" among conglomerates and examining the potential ways to solve the issue. Our paper complements this literature by showing that entrepreneurial firms (or less diversified firms) can improve innovation likelihood and efficiency by licensing "shelved" projects from large firms.

Second, our paper contributes to the literature on the impact of financing on re-

search and development and corporate innovation.[5] Recently, researchers have started to focus on the pharmaceutical industry. Higgins and Rodriguez (2006) find that stock market return for pharmaceutical acquirers is significant positive and show that the positive return is achieved by bringing in R&D productivity from the target firm to the acquirer. Instead of using the acquisition context, our paper show that there big pharmaceutical companies can encounter innovation inefficiency, which might be improved by licensing the shelved projects to entrepreneurial firms. J. Krieger, Li, and Papanikolaou (2022) shows that pharmaceutical firms may underinvest novel innovation drugs but go for "me-too" drug due to risk aversion. Li, Liu, and Taylor (in press) documents how the common ownership of venture capitalists in startups can affect the innovation outcome of the invested pharmaceutical companies. Our paper is also related to Cunningham et al. (2021), which shows the pattern of large companies conduct "killer acquisitions" of small and innovative firms with the purpose of stifling competition. Our paper examines the opposite direction - small companies licensing projects from large firms - and how small companies might bring efficiency in innovation and drug development. Other papers have used the drug development info Aghamolla and Thakor (2021) a private firm's decision to go public affects the IPO decisions of its competitors. Guedj and Scharfstein (2004)

Our paper is related to the literature on the licensing of patents and drugs. Except a few papers examining the licensing and trading of patents (Akcigit, Celik, & Greenwood, 2016; Han, Liu, & Tian, 2020; Ma, Tong, & Wang, 2021), there have been very limited research on the licensing of drug development despite its economic importance. To our best knowledge, Hermosilla (2021) is the only paper that studies drug licensing activity. However, Hermosilla (2021) mainly focuses on the licensing events

[5]Many papers have looked how financing frictions and types of investors might impact innovation efficiency and outcome. Some examples include cash flow and external equity (Brown, Fazzari, & Petersen, 2009), bank distress Nanda and Nicholas (2014), VC investors' tolerance of failure (Tian & Wang, 2014). See Kerr and Nanda (2015) for a survey on this strand of literature.

of failed late-stage drug projects (i.e., those events happened after the failure of Phase 3 trials) from biotech startups to large corporations. We study a completely different group of licensing events where the large companies out-license the "sleeping" projects to biotech startups and examine whether startup licensors might add efficiency to the drug development process.

3 Institutional Background

3.1 Drug Development, Startups, and Venture Capital

The pharmaceutical industry is well suited to investigate the innovative efficiency of startup companies for the following reasons. First, the biopharmaceutical industry is a very active industry for startups. For example, Statista documents that the distribution of startups in the life sciences and healthcare industry (6.8% of all startups) is second only to the fin-tech industry (7.1% of all startups).[6] Second, the industry also attracts a great deal of venture capital. For example, the Wall Street Journal's VC tracking tool displays about 1000 VC deals completed in health care of which the biopharmaceutical industry had the lion's share attracting about $15 billion in VC funding in 2018. Third, the regulatory requirements and common practices within this industry make possible the availability of granular product-level data on a firm's entire product portfolio. This allows us to identify the competing projects, the firm's exposure to any of its therapeutic markets, and the type and timing of innovative activities at the product level. Finally, product licensing is a common practice within the industry, This is especially relevant for startup firms with financial constraints since drug development through licensing costs significantly less than undergoing the entire drug development process organically.

[6] According to the report published by Statista Research Department. The report is available at https://www.statista.com/statistics/882615/startups-worldwide-by-industry/.

3.2 FDA Clinical Trials and Approval

Firms developing drug projects for US markets must follow a structured regulatory multi-step process before obtaining FDA approval. The FDA does not unconditionally approve a drug, instead, it approves a drug for a certain medical condition (e.g., Merck's drug Keytruda was approved for Melanoma). This means that the drug development process must demonstrate the safety and efficacy of a drug in addressing a medical condition. The drug development process involves three broad steps: pre-clinical research, clinical (in-human) testing, and new drug applications. Underlying each broad step are development stages designed to achieve certain goals. The first broad step, pre-clinical research, includes two development stages that cost between $1 to $7 million, on average, and require 3 to 8 years to complete Garfinkel and Hammoudeh (2020). Pre-clinical research starts with drug discovery, where thousands of molecules are screened before arriving at only a handful of promising candidates. These candidates then move on to the pre-clinical stage where they are tested in labs and on animals. Once a candidate drug demonstrates promising results in pre-clinical research, it then moves on to - the more costly and lengthy - clinical trials. The first stage of clinical trials, Phase-I, tests a drug's safety in a small sample of 10 to 50 volunteers. If a drug proves safe in humans, it then moves to phase-II clinical trials, where its safety and efficacy are tested in a larger sample of 50 to 200 volunteers. Drugs with strong phase-II evidence move to phase III, where the safety and efficacy of the drug are tested in a very large sample of 200 to 3,000 volunteers. Once clinical trials are complete, and the sponsoring firm is satisfied with the evidence, a new drug application is filed with the FDA. FDA advisory committees meet periodically to review a drug's findings from clinical trials and approve (or deny) a drug for sale in US markets for a certain medical condition. Noteworthy, following the FDA Amendments Act of 2007, firms developing drugs for US markets are required to publicly disclose the findings from clinical trials

on clinicaltrials.gov.

3.3 Drug Licensing

Licensing means that the "licensor" (i.e., the originating or inventing company) transfer the rights to develop and commercialize a drug project to a "licensee" (i.e., the buying or the in-licensing company). The licensing market is sizable, continuously growing, and therefore, economically relevant. Referred to as "biobucks" in the pharmaceutical industry, the dollar amount of US and European-based licensing deals reached $43 billions in 2010 and $57 billions in 2016.[7] The licensing not only transfers the intellectual property, but often time the founding scientists and research team will also move with the project (Danzon, Nicholson, & Pereira, 2005; Mason, Savva, & Scholtes, 2008).

There are several reasons why firms engage in drug licensing. Most importantly, organic drug development is costly, e.g., a recent study by DiMasi, Grabowski, and Hansen (2016) estimates the cost of drug development to be about $2.6 billion. This costs are especially problematic to resource-constrained startups. Drug licensing offers a much more affordable solution; the licensor transfers the rights to develop and commercialize a drug project in return for royalties. These royalties are normally reasonable, e.g., startup Spero licensed an antibiotic from the large Japanese firm Meiji Seika for an upfront cost of $600,000 and with up to $3 million in milestones. Second, licensing allows both parties to share the risk of drug development. Third, licensing provides startups with a faster path to profitability since the licensed projects have normally completed a few development stages. Furthermore, licensees also benefit from the knowledge spillovers that comes with licensing projects from large firms with established labs and high quality scientists. Finally, licensing allows licensors to benefit

[7] According to the EY Report, "Beyond borders: The global biotechnology report in 2017." The report is available here: https://assets.ey.com/content/dam/ey-sites/ey-com/en_gl/topics/life-sciences/life-sciences-pdfs/ey-biotechnology-report-2017-beyond-borders-staying-the-course1.pdf.

from projects shelved for reasons not related to drug efficacy. For these reasons, drug licensing is a very common practice that normally allows both firms to benefit.

4 Data

This section first describes the data used to construct the samples. Next, it details the procedure for creating the licensor-licensee drug development sample. The procedure for creating the two control samples is then discussed. Finally, it describes the variables used in the analysis.

4.1 Data Description

We use Cortellis for drug development data. Cortellis is an industry-competitive repository on drug development and is commonly used in the literature (see Hermosilla (2021) and J. L. Krieger (2021)). Cortellis regularly collects and refines drug development information from different sources including conferences, financial statements, and other public resources (e.g., clinicaltrials.gov). The data identifies all the medical conditions that a drug is intended to treat. The FDA reviews the clinical trial findings of a drug intended for a certain medical condition.[8] The FDA will only approve the drug for sale in the US market if the evidence from clinical trials provides evidence in favor of the safety and efficacy of a drug in addressing a medical need. A single drug can be developed and approved for several medical conditions, however, the developing firm would need to demonstrate the safety and efficacy of the drug in addressing each indication by conducting separate clinical trials. The Cortellis data provides detailed description of the development history of a drug-indication combination. Importantly, Cortellis

[8]In this paper, we use the following terms interchangeably: therapeutic market, medical condition, ICD market, indication, disease, illness, and product market.

identifies all the firms that developed the drug at any point in time.[9] Cortellis also reports instances where a drug was licensed, the date of licensing, and the licensor and licensee. We use this information to construct the licensing drug development data described in Section 4.2 below.

We make two corrections to the Cortellis dataset. First, inconsistencies sometimes exist in the word description of medical indications as Cortellis collects information from various sources. For example, the two different Cortellis indications liver cirrhosis and liver disease refer to the same medical condition. This poses a challenge for us since we wish to characterize competition within each market and identify the competing products. We map Cortellis indications to the established and standardized ICD-10 diagnostic codes. Drug projects operating in the same ICD-10 code are considered competitors. Second, companies in the pharmaceutical industry often cease to operate under a certain business name. This could be due to several reasons, e.g., acquisition, name change, bankruptcy, restructuring, etc. We supplement the firm information in the Cortellis data by matching the Cortellis' firm names to the SDC Platinum merger data. We ensure that a given drug is assigned to the correct owner each year.

Finally, we identify companies that received VC backing. We match the refined Cortellis sample to the SDC VC data. We collect the VC backing of startups from the VentureXpert dataset.

4.2 Licensee-Licensor Sample Construction

The objective of our study is to examine the innovation efficiency of startups' licensed projects from large and established pharmaceutical companies. This objective guides our choice of focusing on drug projects out-licensed by large firms and not by startups.

[9]While detailed drug development data occurring before 2007 is available for some companies, we focus our sample on drug development after 2007 when the passing of the Food and Drug Administration Amendments Act in 2007 required firms to report the findings from clinical trials no later than one year after their completion.

We exclude startup licensors because startups with promising organically developed projects often seek collaboration opportunities with large more resourceful firms.[10] The "small-to-big" licensing activity is often motivated by significantly different factors relative to those motivating "big-to-small" licensing. For example, large firms with more experience and resources can afford to be selective by licensing higher quality projects and negotiating more favorable licensing terms. Furthermore, large firms may preempt future competition from highly similar competing projects (developed by smaller firms) by acquiring (or licensing) and discontinuing those projects (see Killer acquisitions). On the other hand, small financially constrained firms may not have the same negotiation power and may therefore settle for drug projects shelved by these large firms. Anecdotal evidence suggests a recent increasing trend of startup licensing of large firm shelved products. Our goal is to study whether startup licensees increase the efficiency of the innovation process by reviving otherwise dead projects.

In most cases, when a drug-indication combination is licensed, the original owner ceases all development activity around the same time that the licensee begins. Cortellis provides detailed information on drug development for each of the licensor and licensee separately. This allows us to examine the development activity of startups after the licensing event.

We construct a large sample of licensor-and-licensee drug development by applying the following filters:

- The licensor must have reported the earliest available record for any of the drug indications. We drop drugs where a licensor begins development after a licensee (these are less than 1% of the sample and involve convoluted collaboration arrangements).

[10] For a salient example on this, the German biotechnology company, BioNTech, entered a collaboration agreement with Pfizer to develop the effective Covid-19 mRNA vaccine.

- The licensor must cease drug development shortly after the licensing event (up to 4 quarters after). We drop drug indications where the licensor resumes development after the licensing event. Again, these are usually non-traditional licensing arrangements such as a joint venture or a specific partnership.

- The drug must still be under clinical development on the licensing date. We drop drug indications where FDA approved products are licensed because no further clinical development is possible after FDA approval.[11]

- We use a stringent definition for a startup. A startup must (1) be smaller in size with fewer than 20 total projects (i.e., drug indications), (2) must be relatively new, no older than 8 years, and (3) must have received VC funding in the last 4 years.

- We exclude all drug indications where the licensor is a startup. Note that we still include drug indications where both licensor and licensee are large firms. This provides us with a comparable control group.

- We do not limit our study to drug projects in a certain stage of development. that is, we allow drug projects in the sample at any stage of development (these are drug discovery, pre-clinical trials, Phase-I clinical trials, Phase-II and Phase-III). The relatively small sample of Big to Small licensing events poses a statistical power problem when focusing exclusively on one stage).

- We identify about 400 drug indication licensing events where licensor drug development data exists at least 2 quarters before the licensing event, and at least 2 quarters of licensee data after the event. Of the 400, about 70 drug indications are licensing by a startup.

[11] One exception is Phase 4 clinical development. However, this is much less common and normally conducted for monitoring the safety of a drug in larger populations (monitoring for adverse effects in certain subgroups).

4.3 Construction of the Control Sample

To identify whether startups are more efficient in developing projects licensed from large firms (herein big to small), we compare the development activities of their projects to similar projects that do not experience the "big to small" licensing event (i.e., the counterfactual projects). Ideally, these counterfactuals would help inform us about the drug development efficiency in the absence of startup licensing. Our analyses include three such counterfactuals.

First, as explained above in Section 4.2, we use drug projects licensed from a large firm to another large firm (herein big to big), and operate within the same therapeutic market, as counterfactual projects. In using this counterfactual group, we are effectively comparing the development efficiency of startup licensees to that of big licensees. If we hypothesize that startups are more efficient because they focus on developing the small number of projects in their portfolio, then we would expect to see a positive and significant relationship between innovation success and startup licensing. Note that in our main analyses below, this counterfactual group is used in conjunction with one of the two control groups described below.

The second group of counterfactuals is created by first retaining all drug indications with one total developing firm (i.e., the drug originating firm maintained ownership and never out-licensed the drug). Next, we match treatment licensed projects to all single-developer (i.e., control) projects within the same therapeutic market. Finally, we drop all treatment projects if no control projects within the same market are present. This creates an unbalanced panel with wide variation in firms, markets, and projects.

The matched sample is constructed by matching each treatment project to a comparable control in the same market and undergoing the same stage of development. Moreover, the control project must have started development within five years of the licensing date for the treatment drug, and must also be developed by a firm in the

same size quartile as the treatment licensee firm. Size is measured as the total number of drug projects owned by a firm. Finally, we randomly select one project from a pool of all potential controls that satisfy the above criteria.

Figure A1 displays an example of a treatment drug and its three corresponding controls. All projects in this example target the prostate cancer market. The treatment project was originally developed by Johnson and Johnson (J&J), and was out-licensed in 2016q3 to startup Tracon, which initially licensed the project in the discovery stage and advanced the project to phase-II trials by 2017q2. The figure shows the corresponding control groups. The first group, named Counter Factual Group, contains projects in the same market that were licensed by large firms, e.g., a project out-licensed by GlaxoSmithkline to Novartis. The second group, named Control Drug Projects Group 1, contains all projects developed by a single firm (i.e., never licensed) in the same market. Each treatment project is matched to two control projects: one for the treatment project under the licensor (Progenics's project), and another for the treatment project under the licensee (Madison Vaccines's project). The last control group is constructed by selecting a single project from a pool of potential controls that are developed by a single firm and share the following with the treatment project: market, initial development stage, project age, and firm size. As with Control Drug Projects Group 1, a treatment project is matched to two control projects in this group: one for the treatment project under the licensor (Bayer) and another for the project under the licensee (MetCure Therapeutics).

[Insert Figure A1 about here]

4.4 Summary Statistics

Table 1 presents the summary statistics of our sample. In our baseline (i.e. general) sample as shown in Panel A of Table 1, we have 81 treated drug projects that have

been licensed from big pharmaceutical companies to startup biotech firms. 37% of the treated projects have experienced some progress into the next FDA clinical trial phase and 11% of them are finally approved by the FDA. For the general sample, we have 17,633 control drug projects with 18% of them having progress to the next phase and 3% finally approved by the FDA and launched to the market. In Panel B, we report the summary statistics for an alternative robustness sample with more closely matched treatment and control drug projects is used. For each treatment project, a control project is randomly selected from a pool of all potential controls in the same ICD-10 therapeutic market, with the same stage of development and drug age, and are developed by a similarly sized firm. Control drug projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm throughout the sample period.

[Insert Table 1 about here]

We further look into what factors determine the licensing decisions both for the licensor companies and the licensee companies. In Table 4, we report the summary statistics on the characteristics of drug projects.

5 Empirical Analysis and Results

5.1 Empirical Design

To study whether drug projects licensed from large pharmaceutical companies to biotech startups experience an increase in the likelihood of having development progress, we compare these drug projects with "comparable" drug projects that are either being licensed among large pharmaceuticals or never licensed and under development within

large pharmaceuticals. Specifically, we run regressions based on the following equation,

$$Innovation_{p,q} = \beta_1 Startup_{f,q} * Licensed_{p,q} + \beta_2 Startup_{f,q} + \beta_3 Licensed_{p,q} + \theta_f + \rho_m + \gamma_p + \phi_q + \epsilon \quad (1)$$

where p indexes drug project, q indexes calendar quarter, f indexes firm, and m indexes market. Innovation is an indicator identifies when a project experiences one of two types of innovation: Drug Development is equal to one in the quarter that a project advances to the next stage of development, and is equal to zero so long as it stays in the same stage of development. Drug Approval is equal to one in the quarter that a project receives FDA approval-for-sale, and is equal to zero as long as the project is under development. $Startup_{f,q}$ is an indicator that identifies whether the firm developing the focal drug is a startup. Firms classified as startups must satisfy three criteria: (i) the firm must have received VC funding within the last 5 years, (ii) the firm must be 5 years old or younger, and (iii) the firm must own no more than 20 projects of which none are approved-for-sale. Since a startup firm may not be classified as a startup later on in the sample, we define the Startup indicator using data in the earliest available quarter for each drug in the sample. $Licensed_{p,q}$ is an indicator that identifies whether a drug project is licensed. This indicator does not vary within project, i.e., projects are either licensed or not. Once a drug indication is licensed, it is considered a new project developed under the licensee. The coefficient, β_1, in front of $Startup_{f,q} * Licensed_{p,q}$, represents how much more innovation outcome does a drug indication gain after it is licensed from a large company to a startup.

The treatment group includes drug indications that are originated by a large company and licensed to a startup. The control drug indications include those that have never been licensed (either developed by large companies or startups) and those that have been licensed to a large company.

We are aware of the potential endogeneity issue that potential unobservable characteristics might be correlated to both the licensing decision as well as the drug development efficiency and success. For example, the technical barrier for developing a drug indication is not very high and at the same time is not very profitable for the large company to develop itself but for a startup, this drug indication, therefore, is more likely to be licensed out but at the same time more likely to have drug development progress after licensing. We include several types of fixed effects try to absorb these unobservable characteristics that might bias our estimates. θ_f are indicators for each developing firm, controlling the unobservable characteristics of firms' quality. ρ_m are ICD-10 therapeutic market indicators. γ_p are drug level fixed effects and include indicators for a project's age, vintage year, and originating firm. We include γ_p to control for the characteristics of specific project that might be correlated to both the licensing decision and the innovation outcome. For example, some projects that might be easier to develop and are more likely licensed out. Finally, we include calendar time fixed effects, ϕ_q, to control for unobservable time-specific shocks.

We start with the baseline regressions where we keep all the drug indications originated by large companies. To further ensure that the treated drug projects are indeed comparable to the control project, we then closely match treatment projects with control drug projects. We randomly select from a pool of all potential control projects for a treatment project in the same ICD-10 therapeutic market, with the same stage of development and drug age, and are developed by a similarly sized firm. We also require that these drug projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm throughout the sample period.

5.2 Baseline Results

We start by analyzing whether licensing from a large pharmaceutical company to a biotech startup improves the likelihood of a drug indication making progress in the development, such as passing a Phase I FDA clinical trial. We then examine whether the licensing process improves the likelihood of receiving FDA approval to launch the drug to market.

Table 2 presents the OLS regressions with the dummy variable for making any progress in drug development process (i.e., progressing to the next clinical trial phase). In column 1, only the drug project's developing firm fixed effects and current quarter fixed effects are included. We include the fixed effects of the originator firm of the drug indication to control for the unobservable characteristics on the originating firms' quality. We add the quarter fixed effect to control for unobservable time-specific shocks. In column 2, additional fixed effects for the drug project's therapeutic market. In column 3, we add indicator variables for the drug project's age as well as the indicators for the project's starting quarter. In column 4, we also include the fixed effects for the originating company for a drug indication. Across the four columns, $Startup_{f,q} * Licensed_{p,q}$ is positive and statistically significant at 1% significance level, suggesting that the drug indications licensed from large pharmaceutical companies to biotech firms experience a greater increase in the likelihood of drug development progress compared other drug indications not experiencing "big to small" licensing event. The economic magnitude shows that these projects licensed from large pharmaceutical companies to biotech startups enjoy a 2.6% to 3.4% greater likelihood of progressing to the next phase of the FDA clinical trials compared to projects that are either licensed among large pharmaceuticals or those that are never licensed and developed under large companies.

[Insert Table 2 about here]

In Panel B of Table 2, we substitute the dependent variable to be the dummy

variable representing getting the FDA approval of the drug indication to the market and repeat the analyses in Table 2. We find similar results that drug indications that are licensed from "big to small" are associated with a significantly greater probability of receiving FDA approval compared to other drug projects. In other words, the "big to small" licensing event leads to about 1% to 1.5% increase in the likelihood of getting the FDA approval.

Some may still worry that the projects licensed from large pharmaceuticals might be very different from the ones being licensed from large to large companies or those never licensed projects, and the differences among these projects could drive our previous results. For example, large companies might be willing to out-license projects that are more likely (or easy) to progress to startups with the goal of getting more licensing fees. To address this concern, we use an alternative robustness sample with more closely matched treatment and control drug projects is used. For each treatment project, a control project is randomly selected from a pool of all potential controls in the same ICD-10 therapeutic market, with the same stage of development and drug age, and are developed by a similarly sized firm. Control drug projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm throughout the sample period. We repeat our analysis in Table 2 and present the results of using this alternative sample in Table 3. The sample size of this analysis shrinks to around 21,000 with every treatment project now narrowly matched with a similar project. From this table, one can observe that the main coefficient estimate of interest *Startup*Licensed* is positive and statistically significant in all columns. The results in Table 3 confirm our previous findings.

[Insert Table 3 about here]

5.3 Which Projects are Licensed from Large Firms to Startups?

Our finding that big-to-small licensed projects are more likely to be developed and approved may seem counter-intuitive. That is, a critical reader may wonder why large resourceful firms choose to out-license such "good" projects and split the profits with a smaller firm. Unfortunately, our data does not enable us to answer such a question. Firms may out-license projects for various reasons (e.g., strategic decision, economic feasibility...etc.). Furthermore, firms are often reluctant to share details relating to abandoned innovation that is subsequently out-licensed (see for example J. L. Krieger (2021)). Instead, we could examine the characteristics of these big-to-small projects and compare them to those of the licensor's other projects. Understanding these characteristics may provide insights on some of the factors that drive a licensor's decision to out-license.

To help us understand the characteristics of big-to-small projects and compare them to the drug portfolio of the licensor, we create a cross-sectional sample that includes only the licensor's projects and only in the quarters where that licensor out-licensed a project, regardless of whether the licensing was big-to-big or big-to-small. For each project in this sample, we create variables that measure characteristics at the drug-level, firm-market-level, and market-level. The resulting sample is summarized in Panel A of Table 4. 1.1% of observations correspond to a big-to-small project (Startup Licensed), 5.4% to big-to-big projects (Big Firm Licensed) and 93.5% to never-licensed projects (NeverLicensed). The average project age in a licensor's pipeline (Ln(Project Age))is about 14 quarters, and the median is about 9. About 40% of a licensor's projects use technologies that were not previously used by any of that licensor's other projects (New Technology)). Licensors allocate about 4% of their drug project portfolio to each market they target (Firm-Mkt % All Projects). The

descriptive statistics suggest that licensors are large diversified firms with substantial variation in the characteristics of the projects in their portfolios. This variation may be useful in isolating some of the unique characteristics of big-to-small projects.

We investigate this in multivariate tests. We create an indicator, startup licensed, equal to one if the project was big-to-small, and equal to zero for big-to-big and never-licensed projects. We next regress this indicator on variables that measure characteristics at the drug-level, firm-market-level, and firm-level. We run OLS regressions using the following model:

$$Startup\_Licensed_{p,q} = \beta_1 DrugChar_{p,q} + \beta_2 FMktChar_{m,q} + \beta_3 MktChar_{m,q} + \theta_{fm} + \phi_q + \epsilon \quad (2)$$

[Insert Table 5 about here]

where p indexes drug project, q indexes calendar quarter, f indexes firm, m indexes market, and mB indexes the broad category of the medical condition targeted by the drug. DrugChar, FMKTChar and MktChar are variables on characteristics measured at the drug level, firm-market level and market level. The regressions include firm times broad market fixed effects to control for the unobservable variation that influence a firm's decision to out-license in a certain market, and calendar quarter fixed effects to control for time-specific shocks.

The results are reported in Table 5. The coefficient of Ln(project age) suggests that older projects are more likely to be licensed off to startups. This lends support to our prediction that startups complement the innovation of large firms by reviving abandoned projects. The results also suggest that licensors are more likely to give startups projects that use a new technology, or targets a new market with lengthy approval times and lower revenues. Overall, these results suggest that large firms

are more likely to license off projects that fall outside the firm's expertise. These projects appear to target markets with more challenging externalities such as lengthy development times and lower revenues. We conjecture that licensors abandon such projects because of the high risk (introduced by the inexperience) and the low reward, and choose to share its risk with startups who may find such a trade-off feasible.

We next rerun the same tests above only using the licensee's drug portfolio. We construct a cross-sectional sample of projects owned by licensees in the first quarter that the licensee started developing a big-to-small or a big-to-small project. For each licensee-quarter in the sample, there are three types of projects; big-to-small, big-to-big and never-licensed (i.e., originated by the licensee). We create an indicator, startup licensed, equal to one if the project was big-to-small, and equal to zero for big-to-big and never-licensed projects. We summarize this sample in Panel B of Table 4.

We next use OLS regressions to run the model in equation 2 and report the results in Table 6. The results suggest that relative to big-to-big and never-licensed projects developed by licensees, big-to-small projects are more likely to use a new technology but also more likely to exist in a market where the startup has more exposure. This suggests that startups view the abandoned projects in a large firm's portfolio that target a familiar market as an opportunity to expand market share by offering a wider variety of products with different technologies.

5.4 Additional Tests and Results

One key assumption of the above set of analyses is that the treated drug projects are comparable to the control projects in terms of their trends in the likelihood of progressing to the next FDA clinical trial phase in absence of the licensing events. Even though there is no way to verify this "parallel trend assumption," we show the

dynamics around the licensing events by estimating the following equation:

$$Y_{i,t} = \sum \beta_t Treat_i * TimeRelativeToEvent_t + \text{FIXED\_EFFECTS} + \epsilon \qquad (3)$$

where we replace the *Licensed* dummy with a set of indicators variables representing the time (year or quarter) within the event window and multiplied by the treatment dummy (ever licensed).

We start with the annual frequency and show the results of estimating the raw sample in Figure 1 and the matched sample in Figure 2. The likelihood of a drug project progressing to the next FDA clinical trial phase did not diverge prior to the licensing event as the 95% confidence intervals all covers zero before the event. The difference in the likelihood of progress between the treated projects and control projects enlarges significantly only after the licensing event. provide support for the parallel trend assumption required by the difference-in-differences approach.

[Insert Figures 1 and 2 about here]

Figures A2 and A3 displays the dynamics under quarterly setting instead of in a annual time frequency. We still find supportive evidence for the parallel trend assumption that prior to the licensing event, there is no significant difference in either the likelihood of progress or getting FDA approval.

To ensure our results are robust to different specification of the estimation models, we run robustness tests in Table 7. In Columns 1 and 2, we conduct Logit estimation with and without the above mentioned fixed effects. We find positive and significant coefficient estimates on the *Startup*Licensed* interaction term as well. In Column 3, we use a Hazard model instead to perform the analysis and find a positive relationship between *Startup*Licensed* and the a drug project progress to the next FDA clinical trial phase. The above results provide suggestive evidence that the licensing process from big firms to startups improves the efficiency of drug development.

[Insert Table 7 about here]

6 Conclusion

In this paper, we study whether startups bring efficiency to innovation compared to large companies. Using drug-development data focusing on the consequence of project licensing from large companies to startups, we find that projects licensed from big pharmaceutical companies to startups have a higher probability of progressing to the next phase, receiving FDA approval, and launching the drug to the market, compared to those originated by big pharmaceuticals but never licensed or projects licensed between big pharmaceutical companies. We further show that the results were not purely driven by the "selection effect" that startups license the "better projects" from big pharmaceutical companies.

We also show that relative to the other (never-licensed) projects in the licensor's portfolio, out-licensed projects are older, more likely to use new technology, and target a new market with longer development times and lower revenues. We also find that startups are more likely to in-license projects that target existing markets but use new technology.

Our paper contributes to the literature on the boundary of firms that when companies become large, there will be frictions that hinder the progress of research and development. Our findings underscore the importance of entrepreneurship and startups in reviving some of the "dusted" projects and improving the launch rate and efficiency of innovation.

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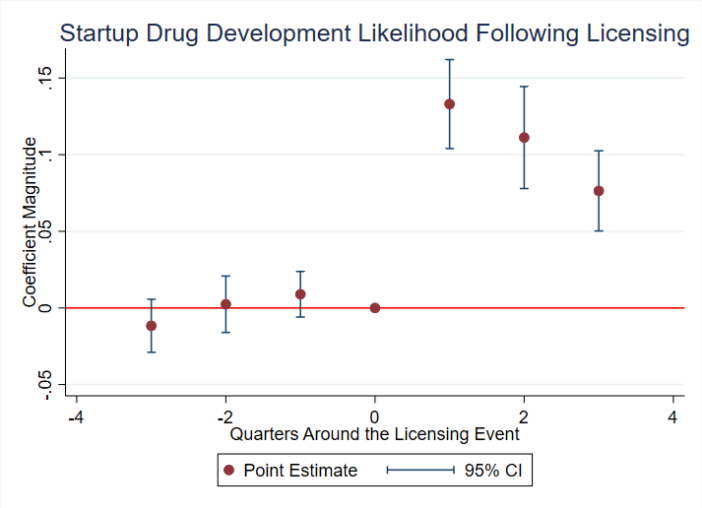
Figure 1. Dynamic Coefficient Plots Around Drug Licensing Events: Raw Sample

This figure displays dynamic trends in the likelihood of drug development (Panel A) and FDA approval (Panel B) for startup licensed projects, around licensing events. The two panels display coefficients from tests that use the raw sample described in Panel A of Table 1, which includes a quarterly panel of treatment and control projects. Treatment projects are owned by a large firm before the licensing event and by a startup (big-to-small) after the same event. Each coefficient is an interactive of the Treatment indicator with an indicator for each of the event years in the period from three years before the licensing event to three years after the same event. Control projects must be in the same ICD-10 market as the treatment project and are either projects licensed by large firms (big-to-big) or projects never licensed (i.e., owned and developed by a single firm). Caps on each coefficient represent the 95% confidence interval for that coefficient's estimate. In both panels, we include the following fixed effects: firm, therapeutic market, calendar quarter, project age, project vintage quarter, and project originator. Standard errors are clustered by drug project. In Panel A, the dependent variable, Development Dummy, is an indicator equal to one in the quarter that a project advances to the next development stage, and equal to zero in all quarters where it remains in the same stage. In Panel B, the dependent variable, Approval Dummy, is equal to one in the quarter when a project is approved-for-sale, and equal to zero in all quarters in which it remains under development.



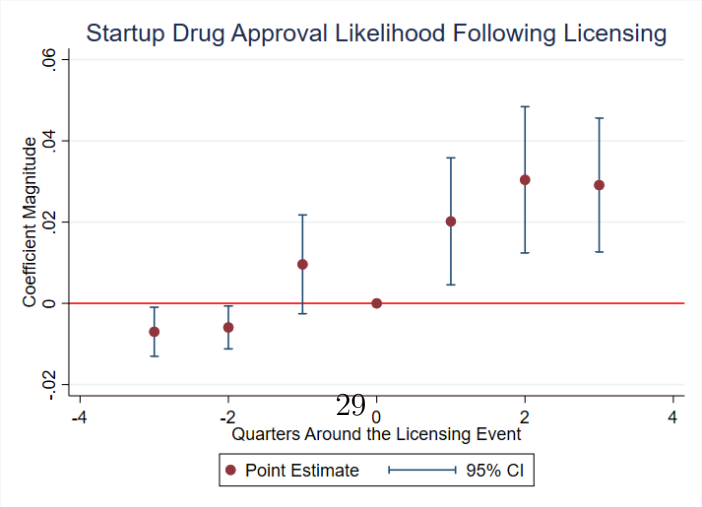
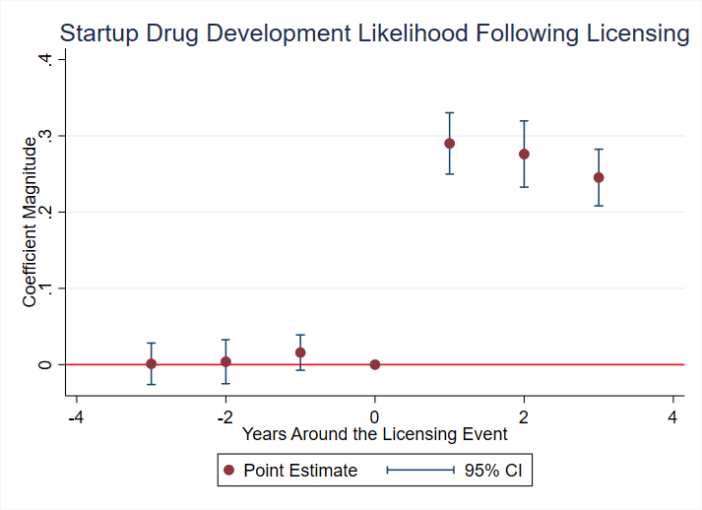


Figure 2. Dynamic Coefficient Plots Around Drug Licensing Events: Matched Sample

This figure displays the same dynamic trends as in Figure 1 only using the Matched sample, which is described in Panel B of Table 1 and includes a quarterly panel of treatment and control projects. Treatment projects are those owned by a big firm before the licensing event and by a startup after. Each coefficient is an interaction between Treatment indicator with an indicator for each of the event years in the period from three years before the licensing event to three years after the same event. For each treatment project, a project is randomly selected from a pool of all potential controls in the same ICD-10 market, with the same stage of development and drug age, and are developed by a similarly sized firm. Control projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm. Caps on each coefficient represent the 95% confidence interval for that coefficient's estimate. In both panels, we include the following fixed effects: firm, therapeutic market, calendar quarter, project age, project vintage quarter, and project originator. Standard errors are clustered by project. In Panel A, the dependent variable, Development Dummy, is an indicator equal to one in the quarter that a project advances to the next development stage, and equal to zero in all quarters where it remains in the same stage. In Panel B, the dependent variable, Approval Dummy, is equal to one in the quarter when a project is approved-for-sale, and equal to zero in all quarters in which it remains under development.



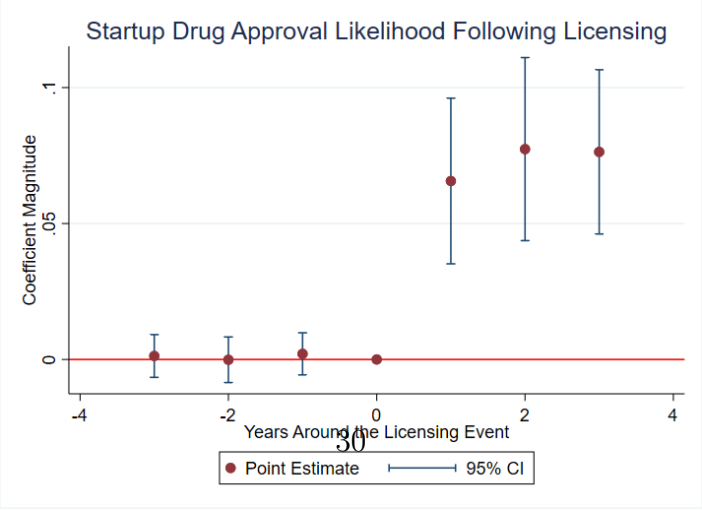


Table 4. Summary Statistics on Drug Characteristics

This table displays summary statistics on the variables used in the drug characteristics tests in Tables 5 and 6. *Startup Licensed*, is an indicator equal to one if the focal project was licensed to a startup and is equal to zero otherwise. *Big Firm Licensed*, is an indicator equal to one if the focal project was licensed to large firm and is equal to zero otherwise. *Never Licensed* is an indicator if the focal project was never licensed, i.e., originated and developed by a single firm. *Ln(Project Age)* is equal to the natural log of the project's age, in quarters. *Early Stage Project* is an indicator equal to one if the project is in the "discovery" stage or the "pre-clinical" stage, and is equal to zero if the project is in any of the three clinical stages of development. *New Technology* is an indicator equal to one if the project uses a technology that the licensor had not used before in any project, and equal to zero if the project's technology was previously used by another project owned by the licensor. *New Mkt* is an indicator equal to one if the project targets a new market that was not previously targeted by any of the licensor's other projects, and is equal to zero if any of the licensor's other projects had targeted that same market. *Firm-Mkt % All Projects* (*Firm-Mkt % Approved*) is a firm-market-level variable with values between zero and one, and is calculated each quarter as the number of a firm's projects (approved-for-sale projects) in the focal project's market divided by the total number of projects (approved projects) owned by the same firm in all markets. *Mkt Competition* (*Mkt # Approved*) is a market-level variable calculated each quarter as the natural log of the number of all projects (the number of all approved projects) in the focal project's market. *Mkt Approval Time* is a market-level variable that measures the average number of quarters a project spends in clinical development before obtaining FDA approval (note that this variable is missing for markets with no approved products). *Mkt Sales* is a market-level variable calculated each quarter as the natural log of revenues by all drugs that target the same market as the focal drug (note that this variable is missing for markets with no approved products and for markets with missing sales data in Cortellis). In Panel A, the analysis sample used in Table 5 is summarized. This cross-sectional sample includes all projects of a licensor in quarters where the same licensor licensed a project to another firm (regardless of whether the licensee was a startup or a large firm). Observations in quarters where no licensing events had occurred are excluded. In Panel B, the analysis sample used in Table 6 is summarized. This cross-sectional sample includes licensee projects in quarters where the same licensee licensed a project from another firm. Observations in quarters with no licensing events are excluded.

Panel A: Statistics on Drug Characteristics in the Licensor's Drug Portfolio					
	Mean	25th Pct	Median	75th Pct	SD
	(1)	(2)	(3)	(4)	(5)
Startup Licensed	0.011	0.000	0.000	0.000	0.102
Big Firm Licensed	0.054	0.000	0.000	0.000	0.227
Never Licensed	0.935	1.000	1.000	1.000	0.247
Ln(Project Age)	2.269	1.792	2.303	2.833	0.769
Early Stage Project	0.309	0.000	0.000	1.000	0.462

Continued on next page

Table 4 – Continued from previous page

	Mean	25th Pct	Median	75th Pct	SD
New Technology	0.391	0.000	0.000	1.000	0.488
New Mkt	0.262	0.000	0.000	1.000	0.440
Firm-Mkt % All Projects	0.042	0.006	0.013	0.031	0.107
Firm-Mkt % Approved	0.012	0.000	0.000	0.009	0.061
Mkt Competition	3.963	2.944	4.043	4.898	1.498
Mkt # Approved	1.819	1.099	1.792	2.708	1.177
Mkt Approval Time	2.592	2.454	2.609	2.815	0.396
Mkt Sales	5.987	4.575	7.234	8.413	3.334

Panel B: Statistics on Drug Characteristics in the Licensee's Drug Portfolio

	Mean	25th Pct	Median	75th Pct	SD
	(1)	(2)	(3)	(4)	(5)
Startup Licensed	0.006	0.000	0.000	0.000	0.078
Big Firm Licensed	0.040	0.000	0.000	0.000	0.196
Never Licensed	0.954	1.000	1.000	1.000	0.209
Early Stage Project	0.328	0.000	0.000	1.000	0.470
New Technology	0.397	0.000	0.000	1.000	0.489
Firm-Mkt % All Projects	0.044	0.005	0.012	0.032	0.111
Mkt Competition	4.050	3.045	4.127	4.977	1.501
Mkt # Approved	2.101	1.386	2.079	2.996	1.221
Mkt Approval Time	2.595	2.450	2.606	2.815	0.348
Mkt Sales	6.646	5.785	7.596	8.898	3.078

Table 1. Summary Statistics

This table displays summary statistics for the samples used in the multivariate analyses below. Number of Projects displays the unique number of drug projects per category. % of Projects Developed (% of Projects Approved) displays the percentage of projects within a category that experienced a drug development (FDA approval) event. Start-up Licensee is the sample of drug projects that were licensed by a start-up firm from an established large firm. Big licensee is the sample of projects licensed by a large established firm from a large established firm. Licensor is the sample of projects that were eventually licensed off, but are summarized while the original owner (i.e., licensor) still owned them (i.e., before licensing them off). Control includes the sample of control projects which is different in the two panels. Finally, Full Sample includes the full sample of drug projects owned by all categories. In Panel A, the sample includes treatment drugs and the general control group drug projects. Treatment drug projects are those licensed by start-ups from large established firms. There are two types of control drug projects used, both must be in the same ICD-10 therapeutic market as the treatment project. The first type are drug projects licensed by large firms from large firms. The second type are drug projects that were never licensed, i.e., drug projects that were owned and developed by a single firm throughout the sample period. In panel B, an alternative robustness sample with more closely matched treatment and control drug projects is used. For each treatment project, a control project is randomly selected from a pool of all potential controls in the same ICD-10 therapeutic market, with the same stage of development and drug age, and are developed by a similarly sized firm. Control drug projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm throughout the sample period.

Panel A: Baseline Sample

	Start-up Licensee (1)	Big Licensee (2)	Licensor (3)	Control (4)	Full Sample (5)
Number of Projects	81	345	425	17,633	18,058
% of Projects Developed	0.37	0.24	0.18	0.18	0.19
% of Projects Approved	0.11	0.07	0.05	0.03	0.04

Panel B: Narrowly Matched Sample

	Start-up Licensee (1)	Big Licensee (2)	Licensor (3)	Control (4)	Full Sample (5)
Number of Projects	64	406	512	954	1504
% of Projects Developed	0.36	0.22	0.19	0.25	0.24
% of Projects Approved	0.14	0.05	0.03	0.06	0.06

Table 2. Drug Development Outcomes Around the Licensing Event

The tests in this table examine the effect of startup licensing on innovation efficiency. The table displays coefficients from OLS regressions using the raw sample described in Panel A of Table 1, which includes a sample of treatment and control projects developed between 2010q1 and 2018q4. Treatment projects are those licensed by startups from large firms (big-to-small). These projects are developed by a large firm before the licensing event and by a startup after. Control projects must be in the same ICD-10 market as the treatment project and are either projects licensed by large firms (big-to-big) or projects never licensed (i.e., owned and developed by a single firm). Startup is an indicator equal to one if the firm developing the focal project is a startup, and equal to zero for large firms. Licensee is an indicator equal to one if the focal project was licensed from a large firm, and is equal to zero if it is developed by the originating firm. Fixed effects are indicated in the bottom 6 rows of each panel and standard errors are clustered by project. t-stats are reported in parenthesis. The significance level represented by the asterisks is as follows: *** p<0.01, ** p<0.05, * p<0.1. In Panel A, the dependent variable, Development Dummy, is an indicator equal to one in the quarter that a project advances to the next development stage, and equal to zero in all quarters where it remains in the same stage. In Panel B, the dependent variable, Approval Dummy, is equal to one in the quarter when a project is approved-for-sale, and equal to zero in all quarters in which it remains under development.

Panel A. Dependent Variable is the Development Event Dummy				
	(1)	(2)	(3)	(4)
*Startup*Licensed*	0.026***	0.028***	0.031***	0.034***
	(0.009)	(0.008)	(0.007)	(0.010)
Startup	0.008***	0.008***	0.025***	0.027***
	(0.003)	(0.003)	(0.002)	(0.003)
Licensed	0.011***	0.009**	-0.018***	-0.003
	(0.004)	(0.004)	(0.003)	(0.005)
Constant	0.015***	0.015***	0.011***	0.011***
	(0.001)	(0.001)	(0.001)	(0.001)
Observations	224,670	224,670	224,635	224,605
R-squared	0.027	0.030	0.256	0.262
Firm FE	Yes	Yes	Yes	Yes
Quarter FE	Yes	Yes	Yes	Yes
Market FE	No	Yes	Yes	Yes
Drug Age FE	No	No	Yes	Yes
Drug Vintage Quarter FE	No	No	Yes	Yes
Originator FE	No	No	No	Yes

Panel B. Dependent Variable is the FDA Approval Dummy				
	(1)	(2)	(3)	(4)
*Startup*Licensed*	0.009	0.010*	0.012**	0.015**
	(1.503)	(1.840)	(2.150)	(2.327)
Startup	0.004***	0.004***	0.007***	0.007***
	(4.545)	(4.505)	(7.300)	(7.041)
Licensed	0.006***	0.005**	-0.003	-0.001
	(2.812)	(2.472)	(1.364)	(0.311)
Observations	224,670	224,670	224,635	224,605
R-squared	0.021	0.025	0.069	0.079
Firm FE	Yes	Yes	Yes	Yes
Quarter FE	Yes	Yes	Yes	Yes
Market FE	No	Yes	Yes	Yes
Drug Age FE	No	No	Yes	Yes
Drug Vintage Quarter FE	No	No	Yes	Yes
Originator FE	No	No	No	Yes

Table 3. Drug Development Outcomes Around the Licensing Event: Progress to the Next Phase

The tests in this table examine the effect of startup licensing on innovation efficiency. The table displays coefficients from OLS regressions using the matched sample described in Panel B of Table 1, which includes a sample of treatment and control projects developed between 2010q1 and 2018q4. Treatment projects are those licensed by startups from large firms (big-to-small). These projects are developed by a large firm before the licensing event and by a startup after. For each treatment project, a project is randomly selected from a pool of all potential controls in the same ICD-10 market, with the same stage of development and drug age, and are developed by a similarly sized firm. Control projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm. Startup is an indicator equal to one if the firm developing the focal project is a startup, and equal to zero for large firms. Licensee is an indicator equal to one if the focal project was licensed from a large firm, and is equal to zero if it is developed by the originating firm. Fixed effects are indicated in the bottom 6 rows of each panel and standard errors are clustered by project. t-stats are reported in parenthesis. The significance level represented by the asterisks is as follows: *** p<0.01, ** p<0.05, * p<0.1. In Panel A, the dependent variable, Development Dummy, is an indicator equal to one in the quarter that a project advances to the next development stage, and equal to zero in all quarters where it remains in the same stage. In Panel B, the dependent variable, Approval Dummy, is equal to one in the quarter when a project is approved-for-sale, and equal to zero in all quarters in which it remains under development.

Dependent Variable is the Development Event Dummy				
	(1)	(2)	(3)	(4)
*Startup*Licensed*	0.043	0.045**	0.056**	0.144***
	(0.027)	(0.021)	(0.022)	(0.029)
Startup	0.003	0.007	0.024*	0.026*
	(0.010)	(0.011)	(0.013)	(0.014)
Licensed	0.013**	0.011**	-0.035***	-0.053***
	(0.005)	(0.005)	(0.006)	(0.013)
Constant	0.020***	0.019***	0.023***	0.023***
	(0.002)	(0.003)	(0.003)	(0.004)
Observations	21,588	21,588	21,586	21,585
R-squared	0.056	0.068	0.324	0.334
Firm FE	Yes	Yes	Yes	Yes
Quarter FE	Yes	Yes	Yes	Yes
Market FE	No	Yes	Yes	Yes
Drug Age FE	No	No	Yes	Yes
Drug Vintage Quarter FE	No	No	Yes	Yes
Originator FE	No	No	No	Yes

Panel B. Dependent Variable is the FDA Approval Dummy				
	(1)	(2)	(3)	(4)
*Startup*Licensed*	0.032***	0.019*	0.022**	0.061***
	(0.012)	(0.010)	(0.011)	(0.014)
Startup	0.002	0.004	0.005	0.005
	(0.001)	(0.004)	(0.006)	(0.006)
Licensed	0.004	0.003	-0.012***	-0.021***
	(0.003)	(0.003)	(0.004)	(0.006)
Constant	0.003***	0.003***	0.005***	0.005***
	(0.001)	(0.001)	(0.001)	(0.001)
Observations	21,588	21,588	21,586	21,585
R-squared	0.062	0.078	0.137	0.160
Firm FE	Yes	Yes	Yes	Yes
Quarter FE	Yes	Yes	Yes	Yes
Market FE	No	Yes	Yes	Yes
Drug Age FE	No	No	Yes	Yes
Drug Vintage Quarter FE	No	No	Yes	Yes
Originator FE	No	No	No	Yes

Table 5. Characteristics of Startup Licensed Projects in Licensor Portfolio

This table examines the characteristics of drug projects licensed to startups relative to the other projects owned by the same licensor. The table displays coefficients from OLS regressions with firm times market fixed effects, calendar quarter indicators and with robust standard errors. The analyses below use a cross-sectional data that includes all projects of a licensor in quarters where the same licensor licensed a project to another firm (regardless of whether the licensee was a startup or a large firm). Observations in quarters where no licensing events had occurred are excluded. The analysis sample has an observation level of firm-project-quarter and includes three projects types, all of which are owned by licensor firms. The three types of projects are: (i) projects licensed to startups, (ii) projects licensed to large firms, and (iii) never-licensed projects. The final sample includes 5,909 projects developed by 283 licensors between 2010q1 and 2020q1, of which 81 projects were licensed to startups. The dependent variable, Startup Licensed, is an indicator equal to one if the focal project was licensed to a startup (type (i)) and is equal to zero otherwise (for types (ii) and (iii)).

	(1)	(2)	(3)	(4)	(5)	(6)
Ln(Project Age)	0.003***	0.003***	0.003***	0.003***	0.003***	0.003***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Early-Stage Project	0.005**	0.002	0.002	0.004*	0.004	0.004
	(0.002)	(0.002)	(0.002)	(0.002)	(0.003)	(0.003)
New Technology		0.009***	0.010***	0.012***	0.011***	0.012***
		(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
New Mkt		0.010***	0.010***	0.006**	0.006*	0.008**
		(0.003)	(0.003)	(0.003)	(0.003)	(0.004)
Firm-Mkt % All Projects			-0.124***	-0.106**	-0.091	-0.088***
			(0.048)	(0.047)	(0.064)	(0.029)
Firm-Mkt % Approved			0.107**	0.091**	0.035	0.039
			(0.045)	(0.045)	(0.035)	(0.036)
Mkt Competition				-0.010***	-0.016***	-0.020***
				(0.002)	(0.003)	(0.003)
Mkt # Approved				0.007***	0.012***	0.016***
				(0.002)	(0.002)	(0.003)
Mkt Approval Time					0.005***	0.005**
					(0.002)	(0.002)
Mkt Sales						-0.002**
						(0.001)
Constant	0.002	-0.004*	-0.001	0.026***	0.025***	0.041***
	(0.002)	(0.002)	(0.003)	(0.006)	(0.008)	(0.011)
Observations	16,396	16,038	16,038	16,038	12,780	11,205
R-squared	0.082	0.205	0.206	0.210	0.254	0.258

Table 6. Characteristics of Startup Licensed Projects in Licensor Portfolio

This table examines the characteristics of licensed drug projects relative to the other projects owned by the same licensee. The table displays coefficients from OLS regressions with firm times market fixed effects, calendar quarter indicators and with robust standard errors. The analyses below use a cross-sectional data that includes all projects of a licensee in quarters where the same licensee licensed a project from another firm. Observations in quarters where no licensing events had occurred are excluded. The analysis sample has an observation level of firm-project-quarter and includes three projects types, all of which are owned by licensee firms. The three types of projects are: (i) projects licensed by startups, (ii) projects licensed by large firms, and (iii) never-licensed projects (originated by either a startup or a large firm). The final sample includes 6,290 projects developed by 291 licensees between 2010q1 and 2020q1, of which 81 projects were licensed by a startup. The dependent variable, Startup Licensed, is an indicator equal to one if the focal project was licensed by a startup (type (i)) and is equal to zero otherwise (for types (ii) and (iii)).

	(1)	(2)	(3)	(4)	(5)
Early Stage Project	0.000	0.000	0.000	0.002	0.003*
	(0.278)	(0.086)	(0.101)	(1.446)	(1.652)
New Technology	0.003***	0.003***	0.003***	0.002**	0.002*
	(2.992)	(2.926)	(3.259)	(2.480)	(1.949)
Firm-Mkt % All Projects		0.180***	0.192***	0.188***	0.242**
		(2.942)	(2.990)	(2.797)	(2.294)
Mkt Competition			-0.001***	-0.001**	-0.002**
			(-2.899)	(-2.451)	(-2.142)
Mkt # Approved			0.000	0.000	0.001
			(0.140)	(0.221)	(1.417)
Mkt Approval Time				-0.002*	-0.001
				(-1.701)	(-0.915)
Mkt Sales					-0.001**
					(-2.003)
Observations	12,693	12,693	12,693	10,688	8,924
R-squared	0.499	0.504	0.504	0.503	0.534

Table 7. Robustness of the Likelihood of Drug Development/Approval and Startup Licensing Tests

The tests in this table examine the robustness of the findings in Tables 2 and 3 to alternative regression models. In both panels, the dependent variable in first (last) three rows is Development Dummy (Approval Dummy), which is an indicator equal to one in the quarter that a project advances to the next development stage (is approved-for-sale by the FDA), and equal to zero in all quarters where it remains in the same stage (in all quarters in which it remains under development). In columns 1, 2, 4 and 5, the sample covers the period from 2010q1 to 2018q4 to control for the right censoring nature of the data. In columns 3 and 6, the sample covers the period from 2010q1 to 2020q1 (since hazard models naturally control for right censoring). z-stats are reported in parenthesis. The significance level represented by the asterisks is as follows: *** p<0.01, ** p<0.05, * p<0.1. Panel A (Panel B) reports results from tests that use the Raw sample (Matched sample) described in Panel A (Panel B) of Table 1. In columns 1 and 4 of both panels, a logistic regression model is used, which includes calendar year fixed effects and cluster standard errors by drug project. In columns 2 and 5, a fixed effect logistic (i.e., conditional logistic) model is used, which includes firm and year fixed effects and robust standard errors. In columns 3 and 6, a Cox Proportional Hazards model is used, which stratifies the sample by market, includes calendar year fixed effects, and clusters standard errors by project.

Dependent Variable	Development Dummy			Approval Dummy		
Model	Logistic	FE Logistic	Hazard	Logistic	FE Logistic	Hazard
Panel A: Raw Sample						
	(1)	(2)	(3)	(4)	(5)	(6)
Startup*Licensee	0.411**	1.000***	0.546***	0.956***	2.003***	1.380***
	(2.381)	(3.721)	(2.784)	(2.636)	(3.196)	(2.934)
Startup	0.245***	0.453***	0.195***	-0.495***	2.125***	-0.500***
	(6.122)	(3.118)	(5.032)	(-4.689)	(4.464)	(-4.447)
Licensee	0.503***	0.145	0.238***	0.831***	0.357**	0.712***
	(6.752)	(1.615)	(3.051)	(6.099)	(1.993)	(4.532)
Observations	224,719	148,767	208,808	224,719	78,307	237,482
Panel B: Matched Sample						
	(1)	(2)	(3)	(4)	(5)	(6)
Startup*Licensee	0.536**	0.717**	0.550*	1.923***	1.799***	2.368***
	(2.141)	(2.306)	(1.808)	(3.694)	(2.624)	(3.167)
Startup	0.085	0.191	0.154	-1.010***	-0.880*	-1.338**
	(0.563)	(0.986)	(0.947)	(-2.671)	(-1.719)	(-2.280)
Licensee	0.179	0.166	0.271**	0.014	-0.010	0.236
	(1.515)	(1.245)	(2.143)	(0.065)	(-0.039)	(0.915)
Observations	21,608	17,693	17,413	21,608	7,268	20,554

Internet Appendix - Not for Publication

Dusting Off the Old Ones: Drug Licensing to Startups, Innovation Success and Efficiency

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Figure A1. An Example of the Matching Between Startup Licensed Projects and Control Drug Projects

This figure displays an example of the matching between startup licensed projects (treatment project) and controls. All projects in this example target the prostate cancer market. The treatment project was originally developed by Johnson and Johnson (J&J), and was out-licensed in 2016q3 to startup Tracon, which initially licensed the project in the discovery stage and advanced the project to phase-II trials by 2017q2. The figure shows the corresponding control groups. The first group, named Counter Factual Group, contains projects in the same market that were licensed by large firms, e.g., a project out-licensed by GlaxoSmithkline to Novartis. The second group, named Control Drug Projects Group 1, contains all projects developed by a single firm (i.e., never licensed) in the same market. Each treatment project is matched to two control projects: one for the treatment project under the licensor (Progenics's project), and another for the treatment project under the licensee (Madison Vaccines's project). The last control group is constructed by selecting a single project from a pool of potential controls that are developed by a single firm and share the following with the treatment project: market, initial development stage, project age, and firm size. As with Control Drug Projects Group 1, a treatment project is matched to two control projects in this group: one for the treatment project under the licensor (Bayer) and another for the project under the licensee (MetCure Therapeutics).

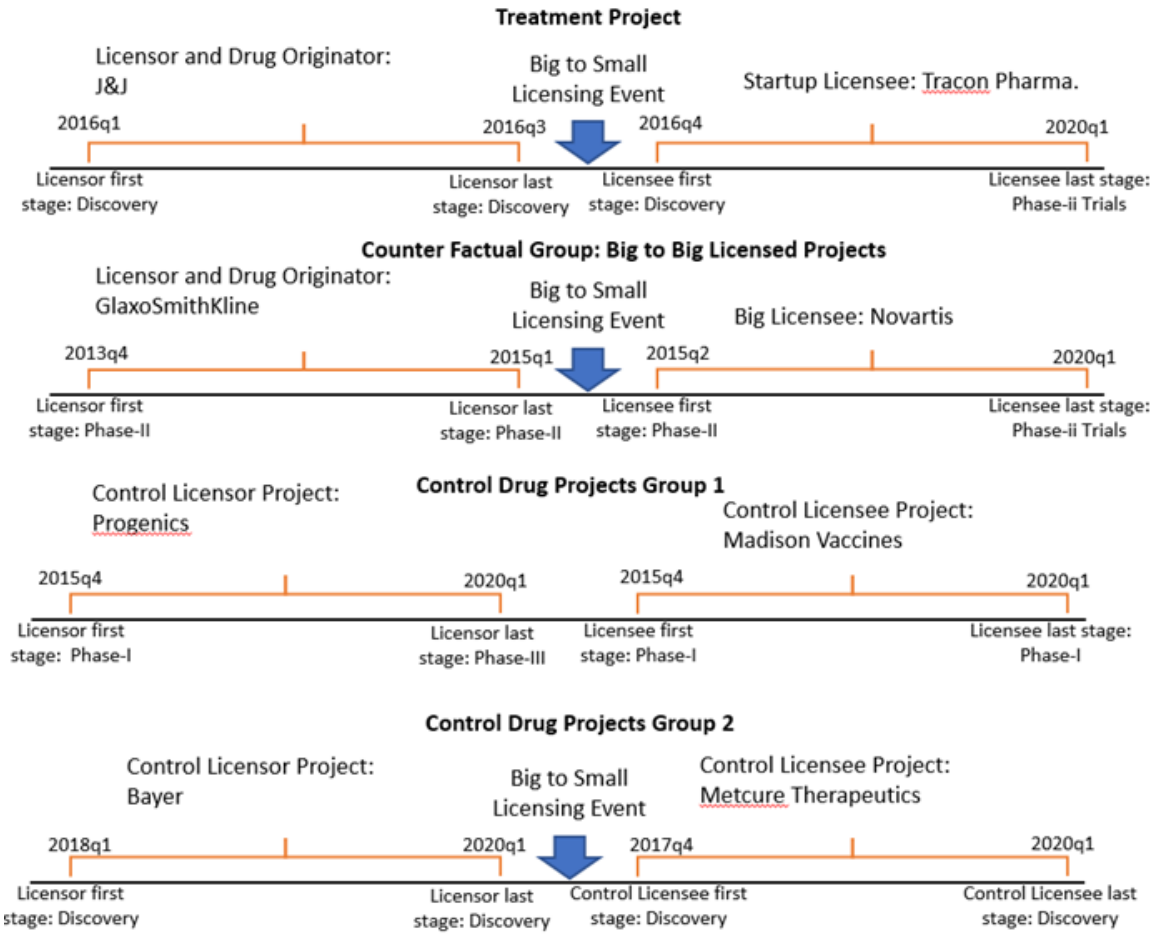


Table A1. Variable Definitions

This table provides the definitions for the variables used in our tests. Panel A, Panel B, Panel C and Panel D provide the definitions of the drug-level variables, firm-market-level variables, market-level variables, and firm-level variables, respectively.

Panel A: Drug-Level Variable Definitions	
Big Firm Licensed	an indicator equal to one if the focal project was licensed to large firm and is equal to zero otherwise.
Early Stage Project	an indicator equal to one if the project is in the "discovery" stage or the "pre-clinical" stage, and is equal to zero if the project is in any of the three clinical stages of development.
Licensee	an indicator equal to one if the focal project was licensed from a large firm, and is equal to zero if it is developed by the originating firm.
Ln(Project Age)	equal to the natural log of the project's age, in quarters.
Never Licensed	an indicator if the focal project was never licensed, i.e., originated and developed by a single firm.
New Mkt	an indicator equal to one if the project targets a new market that was not previously targeted by any of the licensor's other projects, and is equal to zero if any of the licensor's other projects had targeted that same market.
New Technology	an indicator equal to one if the project uses a technology that the licensor had not used before in any project, and equal to zero if the project's technology was previously used by another project owned by the licensor.
Startup Licensed	an indicator equal to one if the focal project was licensed to a startup and is equal to zero otherwise.
Panel B: Firm-Market-Level Variable Definitions	
Firm-Mkt % All Projects	a firm-market-level variable with values between zero and one, and is calculated each quarter as the number of a firm's projects in the focal project's market divided by the total number of projects owned by the same firm in all markets.
Firm-Mkt % Approved	a firm-market-level variable with values between zero and one, and is calculated each quarter as the number of a firm's approved-for-sale projects in the focal project's market divided by the total number of approved projects owned by the same firm in all markets.

Continued on next page

Table A1 – Continued from previous page

Panel C: Market-Level Variable Definitions	
Mkt Approval Time	a variable that measures the average number of quarters a project spends in clinical development before obtaining FDA approval (note that this variable is missing for markets with no approved products).
Mkt # Approved	a variable calculated each quarter as the natural log of the number of the number of all approved projects in the focal project's market.
Mkt Competition	a variable calculated each quarter as the natural log of the number of all projects in the focal project's market.
Mkt Sales	a variable calculated each quarter as the natural log of revenues by all drugs that target the same market as the focal drug (note that this variable is missing for markets with no approved products and for markets with missing sales data in Cortellis).
Panel D: Firm-Level Variable Definitions	
Big Firm	an indicator equal to one if the firm developing the focal project is a large firm, and equal to zero for startups.
Startup	an indicator equal to one if the firm developing the focal project is a startup, and equal to zero for large firms.

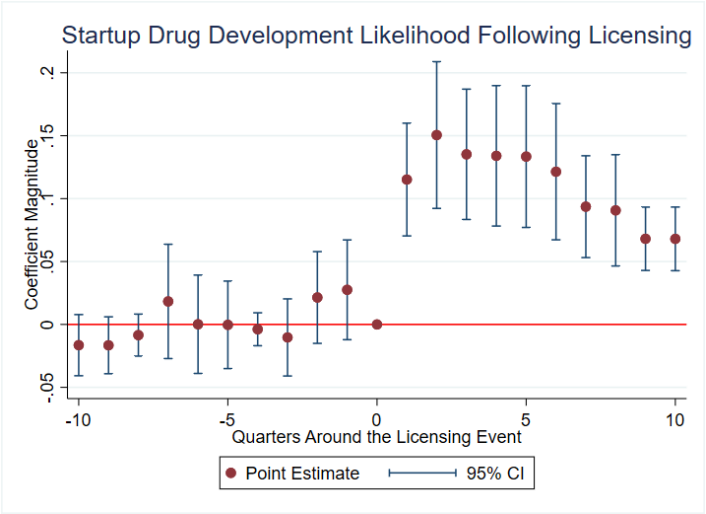
Table A2. Characteristics of Large-Firm VC Licensed Projects (Big-to-Big) in the Licensor's Drug Project Portfolio

This table examines the characteristics of drug projects licensed to large firms relative to the other projects owned by the same licensor. The table displays coefficients from OLS regressions with firm times market fixed effects, calendar quarter indicators and with robust standard errors. The analyses below use a cross-sectional data that includes all projects of a licensor in quarters where the same licensor licensed a project to another firm (regardless of whether the licensee was a startup or a large firm). The analysis sample has an observation level of firm-project-quarter and includes three projects types, all of which are owned by licensor firms. The three types of projects are: (i) projects licensed to startups, (ii) projects licensed to large firms, and (iii) never-licensed projects. The final sample includes 5,909 projects developed by 283 licensors between 2010q1 and 2020q1, of which 78 projects were licensed to startups. The dependent variable, Big Licensed, is an indicator equal to one if the focal project was licensed to a startup (type (ii)) and is equal to zero otherwise (for types (i) and (iii)). The significance level represented by the asterisks is as follows: *** p<0.01, ** p<0.05, * p<0.1

	(1)	(2)	(3)	(4)	(5)	(6)
Ln(Project Age)	0.003	0.003*	0.003	0.002	0.001	0.001
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
Early-Stage Project	-0.020***	-0.022***	-0.022***	-0.022***	-0.027***	-0.026***
	(0.003)	(0.004)	(0.004)	(0.004)	(0.005)	(0.005)
New Technology		-0.008***	-0.008***	-0.009***	-0.012***	-0.012***
		(0.003)	(0.003)	(0.003)	(0.004)	(0.004)
New Mkt		-0.018***	-0.015***	-0.012**	-0.014***	-0.012*
		(0.004)	(0.004)	(0.005)	(0.005)	(0.006)
Firm-Mkt % All Projects			0.051	0.036	-0.032	-0.118
			(0.124)	(0.125)	(0.143)	(0.159)
Firm-Mkt % Approved			0.214**	0.205**	0.180	0.222*
			(0.101)	(0.103)	(0.111)	(0.117)
Mkt Competition				0.001	0.002	0.005
				(0.002)	(0.003)	(0.003)
Mkt # Approved				0.002	0.004	0.001
				(0.002)	(0.003)	(0.004)
Mkt Approval Time					0.001	-0.004
					(0.004)	(0.004)
Mkt Sales						-0.000
						(0.002)
Constant	0.051***	0.054***	0.050***	0.042***	0.040***	0.046***
	(0.004)	(0.004)	(0.006)	(0.009)	(0.014)	(0.016)
Observations	16,396	16,038	16,038	16,038	12,780	11,205
R-squared	0.226	0.376	0.377	0.377	0.374	0.390

Figure A2. Quarterly Time Trends of Startup Licensing and Drug Innovation (Raw Sample)

This figure displays dynamic trends in the likelihood of drug development (Panel A) and FDA approval (Panel B) for startup licensed projects, around licensing events. The two panels display coefficients from tests that use the raw sample described in Panel A of Table 1, which includes a quarterly panel of treatment and control projects. Treatment projects are owned by a large firm before the licensing event and by a startup (big-to-small) after the same event. Each coefficient is an interactive of the Treatment indicator with an indicator for each of the event quarters in the period from 10 quarters before the licensing event to 10 quarters after the same event. Control projects must be in the same ICD-10 market as the treatment project and are either projects licensed by large firms (big-to-big) or projects never licensed (i.e., owned and developed by a single firm). Caps on each coefficient represent the 95% confidence interval for that coefficient's estimate. In both panels, we include the following fixed effects: firm, therapeutic market, calendar quarter, project age, project vintage quarter, and project originator. Standard errors are clustered by drug project. In Panel A, the dependent variable, *Development Dummy*, is an indicator equal to one in the quarter that a project advances to the next development stage, and equal to zero in all quarters where it remains in the same stage. In Panel B, the dependent variable, *Approval Dummy*, is equal to one in the quarter when a project is approved-for-sale, and equal to zero in all quarters in which it remains under development.



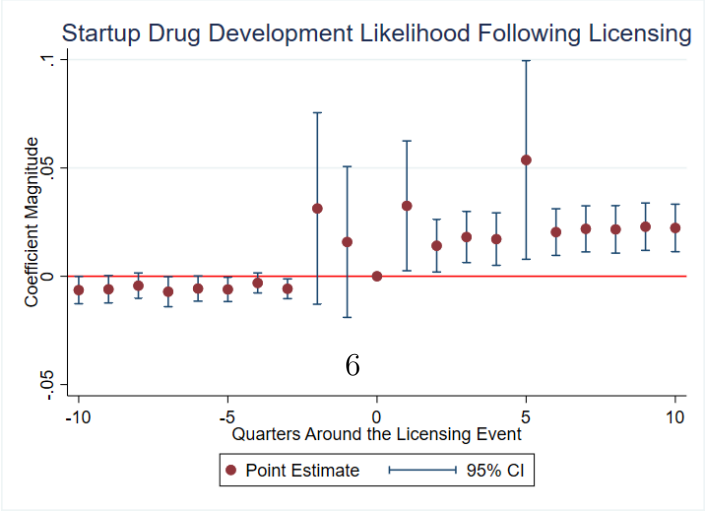


Figure A3. Quarterly Time Trends of Startup Licensing and Drug Innovation (Matched Sample)

This figure displays the same dynamic trends as in Figure A2 only using the matched sample, which is described in Panel B of Table 1 and includes a quarterly panel of treatment and control projects. Treatment projects are those owned by a big firm before the licensing event and by a startup after. Each coefficient is an interactive of the Treatment indicator with an indicator for each of the event quarters in the period from 10 quarters before the licensing event to 10 quarters after the same event. For each treatment project, a project is randomly selected from a pool of all potential controls in the same ICD-10 market, with the same stage of development and drug age, and are developed by a similarly sized firm. Control projects must also have never experienced any licensing events, i.e., they are owned and developed by a single firm. Caps on each coefficient represent the 95% confidence interval for that coefficient's estimate. In both panels, we include the following fixed effects: firm, therapeutic market, calendar quarter, project age, project vintage quarter, and project originator. Standard errors are clustered by project. In Panel A, the dependent variable, *Development Dummy*, is an indicator equal to one in the quarter that a project advances to the next development stage, and equal to zero in all quarters where it remains in the same stage. In Panel B, the dependent variable, *Approval Dummy*, is equal to one in the quarter when a project is approved-for-sale, and equal to zero in all quarters in which it remains under development.