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Market size and innovation: The intermediary role of technology licensing

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ABSTRACT

Previous literature finds that larger downstream markets fuel the innovation of new technologies by incentivizing firms to spend more on R&D. Our evidence shows that larger markets also increase the extent of licensing-based cooperation between upstream innovators and downstream commercializers. This cooperation is valuable because it pools firms' complementary capabilities. Thus, downstream market expansions could positively impact innovative outcomes even holding R&D expenditures constant. Evidence is drawn from the drug candidate licensing market, exploiting the quasi-experimental variation introduced by the enactment of the Medicare Part D program in 2003. A model for the determination of equilibrium commercialization strategies in Markets for Technology rationalizes our finding. In this framework, cooperation gains are proportional to market size but transaction costs are not. Thus, larger downstream markets foster cooperation by reducing the relative importance of the latter. To better match the empirical context, the model extends the canonical "one technology–one application" framework of related work, to the more general case of "composite technologies," which may have more than one end-user application.

1. Introduction

Following the early insights of Schumpeter (1942), Griliches and Schmookler (1963), Schmookler (1966), and Nordhaus (1969), the idea that larger downstream markets may fuel technological innovation has received a considerable amount of scholarly attention. The underlying model is based on the "pull effect:" larger potential market rewards justify larger amounts of R&D investment (inputs), which in turn translate into an increased availability of new technology products for consumers (outputs). We argue that, in addition to sustaining this "pull effect," a larger downstream market may determine innovative outcomes through an impact on equilibrium commercialization strategies. In particular, by increasing the rate of licensing-based cooperation between upstream innovators and downstream commercializers. This cooperation is valuable because it pools firms' complementary capabilities, and could lead to increases in the amount innovative output or total created value, even when R&D expenditures are held constant.

Our argument is supported by empirical evidence from the drug candidate licensing market. These deals articulate inter-firm cooperation aimed at completing the development and commercializing new drug compounds. Typically, cooperating firms include a highly specialized upstream Biotech innovator (out-licensor), and an experienced downstream Big Pharma commercializer (in-licensor). A potentially large value of cooperation can be justified, for example, because a new therapy's development requires significant resources and broad clinical expertise, which Big Pharma in-licensors usually posses but Biotech out-licensors lack (Powell, 1996). For example, after the Biotech firm iTeos out-licensed Cancer targets to Pfizer in 2014, an officer of the former stated that "the oncologic expertise of Pfizer will help enable the acceleration and expansion of the scope of iTeos' IDO1 and TDO2 programs."[1] As implied by this quote and other literature cited in Section 2, this type of cooperation may increase the ROI of R&D expenditures.

Our identification strategy exploits the variation introduced by the enactment of the Medicare Part D program ("Part D") in the US in 2003. This program significantly expanded the insurance coverage of prescription drug expenditures of Medicare enrollees, thus increasing the expected market size for therapies targeting diseases that are more prevalent among the Medicare population (predominantly, elderly people). Following previous research, we construct a measure of shock exposure (or "Medicare orientation") at the targeted-disease level, and merge it to drug candidates in a comprehensive dataset of licensing deals signed between 2000 and 2007. Given the long pharmaceutical development cycles, this relatively short time frame allows us to isolate Part D's impacts on licensing from its subsequent impacts on the supply of "licensable" compounds. Thus, R&D expenditures can be thought as being held constant in our analysis.

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[1] See http://www.iteostherapeutics.com/iTeos-Therapeutics-Announces-License-and-Collaboration-with-Pfizer-Inc.

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Relative to deals that did not include the US within licensed territories, we find that the program's passage increased licensing activity for deals that included it and were associated with relatively high degrees of Medicare orientation. The effect decreases for less Medicare-oriented deals, becoming statistically insignificant for the fifty percent of deals at the bottom of the distribution. We interpret this result as evidence that the downstream market size is a determinant of equilibrium commercialization strategies, with larger downstream markets implying an overall higher rate of cooperation.

To rationalize these results, we draw from the literature on Markets for Technology (henceforth "MFT"; Arora et al., 2001). This literature emphasizes that the potentially large gains of cooperation may not always be materialized due to the existence of significant contracting frictions, or *transaction costs* (Spulber, 2014). Holding R&D expenditures constant, our simple model predicts that a larger downstream market increases cooperation by reducing their relative importance. Thus, the documented increase in licensing activity can only be rationalized if transaction costs are meaningfully large. A calibration of the model is used to illustrate what we call the "intermediary role of technology licensing": by enabling higher rates of valuable cooperation, a larger downstream market increases the industry-wide ROI obtained from R&D expenditures. This increment could be supported by a larger number of commercialized technologies, a higher return for each commercialized technology, or a combination thereof.

An important feature of drug development is that compounds (specific chemical or biological entities) can often be used to treat multiple diseases, which tend to span across therapeutic areas. Each of these applications is called an "indication" in the industry, and requires largely independent sets of clinical trials. Furthermore, licensing deals often bundle multiple indications of a single compound. Concurrently, in-licensing commercializers have heterogenous capabilities — "no company is equally good at developing or selling these molecules in all the different indications" (Longman, 2006). Our results indicate that the Part D shock increased the rate at which more Medicare-oriented indications were licensed through "single-indication" or "unbundled" deals.[2]

To better match this feature of the empirical context, the model extends the canonical "one technology–one application" framework found in the MFT literature, to the more general case of *composite technologies*, which may have more than one end-user application. Each composite technology is formulated as a *technological core* (i.e., a compound). A core's distinct end-user applications are enabled by a set of *sub-technologies* (i.e., indications).[3] Heterogeneous capabilities among in-licensors imply that some cores' different sub-technologies may be best suited to the capabilities of different in-licensors. However, because each licensing deal implies an additional transaction cost, a core's multiple sub-technologies may be licensed as a bundle. By reducing the relative importance of transaction costs, a larger market size increases the share of cooperation gains that are achieved through unbundled licensing. Our calibration study shows that as the downstream market get bigger, a larger share of cooperation and total created value relies on unbundled licensing.

Our work sheds light on the role of downstream market demand in Markets for Technology. Arora and Gambardella (2010) note that this literature has maintained a strong "supply side" emphasis, or "the factors that lead companies to license or sell technology, the implications thereof (..) and the conditions that facilitate the rise of technology specialists." We offer a more panoramic view, where "demand side" in-licensors act as "agents for the commercialization" of applications valued by end-users. Although our analysis does not focus on the individual behavior of firms, we interpret the vigorous cooperation response to the Part D shock as an agile response by these "agents." Carefully interpreted, this agile response also suggests that in-licensors may effectively "weed out" developing technologies "pushed" by innovators, but for which end-user demand does not justify the development and commercialization effort.

In addition to contributing to the broader innovation literature cited above, we also contribute to the body of work studying the rate and direction of pharmaceutical innovation. Previous research shows that larger downstream markets enable higher rates of drug innovation, either measured by R&D expenditures (Blume-Kohout and Sood, 2013; Dranove et al., 2014) or drug approvals (Acemoglu and Linn, 2004; Cerda, 2007; Dubois et al., 2015). Our findings suggest that market size may also mediate the relationship between these two variables.

The remainder of the article proceeds as follows. Section 2 provides background for the drug candidate licensing market, and describes the sources of cooperation gains and transaction costs. Section 3 presents the analytical model. Section 4 describes the Medicare Part D program. In Section 5 we list data sources and describe data processing. Results are presented in Section 6 and conclusions in Section 7.

2. Drug candidate licensing

2.1. Background

Up to the 1980s, drug discovery was primarily conducted through combinatorial approaches, by which millions of compound combinations were tested in order to identify interactions. This process heavily relied on access to "chemical libraries," which stored the results of previous experiments, and greatly expedited the identification of new drug candidates. Their proprietary nature conferred these libraries a role of entry barriers, sustaining the predominant vertical integration of discovery, development, and commercialization observed in the industry until that time (Pisano, 2006).

The biotechnology breakthroughs of the late 1970s and early 1980s opened the door to an alternative route to drug discovery.[4] These advances shed light on the mechanics of human biology, allowing scientists to adopt an "engineering" or "rational design" approach to drug innovation. The entry barriers posed by proprietary chemical libraries weakened, and a fringe of small biotech firms began to discover new compounds.

These events led to the reformatting of the pharmaceutical industry, which transitioned from the fully integrated scheme into a vastly vertically-disintegrated one. In the resulting configuration, large pharmaceutical firms focus primarily on late stage development and commercialization, while biotech innovators focus on the earlier discovery stages.

Owing to the dynamism of basic science, licensing-based cooperation has become an integral part of drug development. The survey

[2] Longman (2006) suggests that the unbundling of indications — labeled as "indication splitting" — is rare in the industry. Nevertheless, in the same article, Longman illustrates the described sources of cooperation gains with the example PDL Biopharma's monoclonal antibody molecule Daclizumab. Daclizumab's Asthma indication was in-licensed by Roche, which has extensive experience developing treatments for respiratory diseases. (From the Roche website (September, 2017): "With nearly 30 years in respiratory research, we are focused on improving outcomes for patients with severe respiratory diseases." See https://www.roche.com.) The Multiple Sclerosis indication was instead in-licensed by Biogen, which specializes on neurological diseases. (From the Biogen website (September, 2017): "As a leading company in the fight against multiple sclerosis, Biogen is applying its expertise to help address some of the most challenging and complex diseases of the brain." See https://www.biogen.com.)

[3] Our definition of composite technologies does not equate to the concept of General Purpose Technologies (GPTs). Whereas GPTs are "characterized by the potential for pervasive use in a wide range of sectors" (Bresnahan and Trajtenberg, 1995), composite technologies have a limited, well-defined set of applications, each of which requires focalized development. In addition, whereas "most GPTs play the role of 'enabling technologies,' opening up new opportunities rather than offering complete, final solutions" (Bresnahan and Trajtenberg, 1995), composite technologies provide a set of complete, final solutions (each embedded on a particular sub-technology).

[4] A full account of these events is beyond the scope of this paper. See Pisano (2006) for an excellent review.