Research Policy xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Research Policy

journal homepage: www.elsevier.com/locate/respol

R&D portfolios and pharmaceutical licensing

Junichi Nishimura [a,*], Yosuke Okada [b]

[a] Faculty of Economics, Gakushuin University, Mejiro 1-5-1, Toshima, Tokyo 171-0031, Japan
[b] Graduate School of Economics, Hitotsubashi University, Naka 2-1, Kunitachi, Tokyo 186-8601, Japan

ARTICLE INFO

Article history:
Received 11 March 2011
Received in revised form 5 March 2014
Accepted 16 March 2014
Available online xxx

JEL classification:
C13
L24
L65

Keywords:
R&D portfolios
Licensing
Pharmaceutical industry
Drug pipelines

ABSTRACT

We examine how R&D portfolios of drug pipelines affect pharmaceutical licensing, controlling firm size, diversity, and competition. The data collected comprises 434 license-ins and 329 license-outs closed by 54 Japanese pharmaceutical companies between 1997 and 2007. We pay special attention to stage-specific licensing by dividing the innovation process into early and late stages. Joint estimates of license-in and license-out using seemingly unrelated regressions (SUR) reveal that drug pipelines significantly affect stage-specific licensing, inducing portfolio effect that lead to smoothing drug pipelines across early and late stages.

1. Introduction

Utilizing market for technology through licensing and other outsourcing arrangement has emerged as key to organize innovative activity: how to coordinate internal and external knowledge using licensing across a firm's boundary reflects strategic position of R&D portfolio at various stages of innovation process (Arora et al., 2001a; Arora and Gambardella, 2010b; Chesbrough, 2003; Narin et al., 1997; Stephan, 1996; Tsai and Wang, 2007).

This paper examines how R&D portfolios of Japanese pharmaceutical firms affect licensing decisions. The pharmaceutical industry is, arguably, the leading industry where market for technology has rapidly grown (Arora and Gambardella, 2010a). Japanese pharmaceutical firms are actively engaged in inward as well as outward licensing, which helps them to introduce new technologies and adjust their R&D portfolios.

In addition, details of pharmaceutical R&D is closely reflected through drug pipelines—drug candidates under clinical testing as well as approved drugs being marketed.[1] Luckily, we can observe drug pipelines quite accurately owing to the rigorous regulatory process of clinical testing: pre-clinical, phase I, phase II, phase III, and post marketing surveillance (PMS), which enables us to measure the state of R&D portfolios.

Drug pipelines may dictate a licensing decision as a result of portfolio adjustment across different stages. Hereafter we refer to this causality as *portfolio effect*. For example, a firm with relatively rich drug candidates at one clinical stage is likely to license out some drug candidates at that stage. In contrast, if the number of drug candidates at some stage diminishes compared with other stages, a firm may accelerate inward licensing at that stage to secure stable cash flow by leveling off the drug pipelines across stages.

From a theoretical point of view, the expected profit of an R&D project reflects its option value, dictating selection and reallocation of managerial resources among projects (Hartmann and Hassan, 2006; Myers, 1984). In a similar fashion, a pharmaceutical firm may realign its R&D portfolio according to the market value of a therapeutic field which varies by treatment satisfaction by new medication, fierce market competition within a therapeutic field, and demographic aging, to name a few.

* Corresponding author. Tel.: +81 3 5992 3649.
E-mail addresses: junichi.nishimura@gakushuin.ac.jp (J. Nishimura), yookada@econ.hit-u.ac.jp (Y. Okada).

[1] The state of drug pipelines can be regarded as a useful proxy for the portfolio of pharmaceutical R&D, because resource allocation among pharmaceutical R&D projects which incur huge cost for clinical test is closely associated with the distribution of drug candidates across therapeutic categories. Unfortunately, we could not utilize detailed data on project-based R&D expenditures. In addition, patent data are not useful because they reflect upstream drug discovery research.

http://dx.doi.org/10.1016/j.respol.2014.03.008
0048-7333/

Chan et al. (2007) provide a theoretical model of project selection that explicitly incorporates R&D pipelines, transaction costs, and downstream complementary assets such as distribution channels and brands. By using a dynamic programming technique, they examine both investment and licensing decisions, indicating that R&D pipelines and downstream complementary assets affect the optimal R&D portfolio as well as the incentive to use the technology market at different R&D stages. Their theoretical study corroborates our empirical motivation to clarify the significant role of drug pipelines in licensing decisions.

Two conflicting strategic effects vary the incentive to license (Arora and Fosfuri, 2003). One is *revenue effect* which enhances a licensor's profit with royalties paid by licensees, and the other is *rent dissipation effect* which erodes a licensor's profit by intensifying competition due to a licensee's entry into the licensor's market. For example, intense competition of R&D or marketing stage makes revenue effect outweigh rent dissipation effect; it raises the incentive to license to horizontal rivals. Firms faced with severe competition are marginally exposed to a small rent dissipation effect by licensing their technologies to rivals. Hence, they would obtain large royalty revenues through licensing due to many potential licensees.

Few empirical studies explore the influence of R&D portfolios on licensing.[2] Most studies in the literature focused on complementary assets that facilitate knowledge absorption as well as exploitation of its own inventions, thereby increasing inward licensing and decreasing outward licensing (Arora et al., 2001a,b; Arora and Ceccagnoli, 2006; Fosfuri, 2006; Gambardella et al., 2007; Kollmer and Dowling, 2004; Montalvo and Yafeh, 1994; Shane, 2001; Teece, 1986).

Another possible conduit of technology transaction is mergers and acquisitions (M&A). Higgins and Rodriguez (2006) suggest that the bleak prospect of drug pipelines induces M&A between U.S. pharmaceutical companies. Using data on 160 pharmaceutical firms' acquisitions from 1994 to 2001, they defined *desperation index* consisting of the state of drug pipelines and their remaining patent lengths, and found that firms with fewer drug candidates likely acquired other firms. Danzon et al. (2007) obtained virtually similar results using M&A data of 383 pharmaceutical firms from 1988 to 2001. It should be noted that there were very few M&As in the Japanese pharmaceutical industry until the late 2000s; within our observation period, M&A is not a serious concern at the present study.

We divided drug pipelines into early and late stages to understand portfolio effect of drug pipelines on licensing across stages. This enables us to pay special attention to the stage-specific determinants of licensing which are not fully explored in the literature. Furthermore, we should regard drug pipelines as endogenously determined; drug pipelines influencing a firm's license decision may be themselves influenced by a firm's license activity. Considering this possibility, we used lagged variables for drug pipelines in estimations.

The decisions of inward and outward licensing are closely correlated with each other (Grimpe and Hussinger, 2009). If portfolio effect exists, inward and outward licensing may be coordinated reflecting a realigned optimal R&D portfolio. Considering this possibility, we jointly estimated equations of both inward and outward licensing at early and late stage using seeming unrelated regressions (SUR).

Our estimates from SUR reveal that drug pipelines significantly affect stage-specific licensing. The Japanese pharmaceutical companies smooth out the state of drug pipelines through licensing. On average, portfolio effect impacts on the propensity to licensing to virtually the same extent as the complementary assets, which has been regarded as the major driver of licensing.

This paper is organized as follows. Section 2 explains our classification of licensing stages and the definition of drug pipelines. Section 3 presents the theoretical and empirical background of the portfolio effect and other factors affecting licensing decisions. Section 4 describes data sources, an overview of pharmaceutical licensing in Japan, and the case of portfolio adjustment through licensing. Section 5 provides our empirical specifications, variable constructions, and basic statistics. Section 6 presents estimation results and discussions. Section 7 concludes the paper.

2. Drug pipelines and licensing stages

New drug development is a sequential process. Fig. 1 presents the typical innovation process of pharmaceuticals. Quite a few drug candidates at the discovery stage are screened for synthesis by chemists and biologists in order to develop concepts for new compounds. Once a new compound has been synthesized, it is screened for pharmacologic activity and toxicity in vitro and in animals (pre-clinical testing), and thereafter in humans.[3] Human clinical testing typically comprises three distinct stages, phase I, phase II, and phase III, each of which involves different types of testing on safety and efficacy. Phase I is performed on a small number of healthy human subjects in order to obtain information on toxicity and safe dosage ranges. Phase II is performed on a larger number of humans who are patients for whom the drug is intended to be prescribed. Phase III involves large-scale trials on patients. The later a clinical trial is conducted, the greater its cost. Therefore, it is important for a pharmaceutical firm to screen promising candidates as efficiently as possible (DiMasi et al., 2003). Next, a pharmaceutical firm submits a list of drug candidates that are supported by phase III clinical testing to the Ministry of Health, Labor and Welfare (MHLW) (pre-registration). An approved drug is subsequently registered and listed with its reimbursement price. Finally, a marketed drug is subject to post marketing surveillance (PMS).

As shown in Figure 1, we divide the drug innovation process into two parts: *early stage* and *late stage*. Following Higgins and Rodriguez (2006), the early stage comprises the pre-clinical phase and phase I, and the late stage comprise all the stages after phase I.[4] Accordingly, we categorize drug pipelines and licensing contracts by the two stages. This distinction between the early stage and the late stage helps to accentuate a strategic effect of drug pipelines on licensing.

It is worth noting three practical reasons for this classification.[5] First, clinical testing at the late stage (phase II and phase III) requires much higher costs than at the early stage (pre-clinical and phase I). Second, a fast-truck clinical testing procedure for life-threatening or highly effective drug candidates (e.g., anti-cancer drugs and orphan drugs) renders classification of drug candidates between phase II and phase III quite obscure and virtually impossible. Finally,

[2] This may be partly because the literature on licensing decisions mainly considers the supply side of technology market (Laursen et al., 2010). As Chesbrough (2003) pointed out, however, understanding both buyer's and seller's incentive is necessary to enhance innovation management. We appreciate the reviewer's suggestion on this remarks.

[3] The Pharmaceuticals and Medical Devices Agency (PMDA) conducts reviews and related services on pharmaceuticals and medical devices for marketing authorization in accordance with the Pharmaceutical Affairs Law in Japan.

[4] In an unreported examination, we included all stages after pre-registration as a third stage. Furthermore, in another unreported examination, we marked the boundary between phase 2 and phase 3. We obtained virtually similar results at a slightly lower significance level compared to the present study. Therefore, we hereafter report the empirical results based on the early/late classification of Fig. 1.

[5] Unfortunately, we found no information on the number of drug seeds at the discovery stage.

Please cite this article in press as: Nishimura, J., Okada, Y., R&D portfolios and pharmaceutical licensing. Res. Policy (2014), http://dx.doi.org/10.1016/j.respol.2014.03.008