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Abstract

We examine how R&D portfolios of drug pipelines affect pharmaceutical licensing, controlling firm size, diversity, and competitors in R&D and product markets. The data collected comprises 329 license-outs and 434 license-ins closed by 54 Japanese pharmaceutical companies between 1997 and 2007. We pay special attention to stage-specific licensing by dividing the innovation process into an early stage and a late stage. Estimates from the fixed-effect GMM model reveal that drug pipelines significantly affect stage-specific licensing. Particularly, the state of drug pipelines is leveled off by license-outs at the early stage and license-ins at the late stage. Theoretical implications are also discussed.

Keywords: R&D portfolios, licensing, pharmaceutical industry, drug pipelines
JEL classification: C13; L24; L65.

1. Introduction

Over the past two decades, utilizing *markets for technology* through licensing and other outsourcing arrangements has emerged as a key to organizing innovative activity (Arora et al., 2001a). The coordination of internal and external knowledge across a firm's boundary is now regarded as the core of R&D management, especially in high-tech industries. Obviously, it is virtually impossible and never desirable for all relevant technologies to be developed by a single firm (Stephan, 1996; Narin et al., 1997; Chesbrough, 2003). It is, therefore, very probable that the incentive to utilize markets for technologies is closely associated with R&D portfolios at various stages of acquisition, accumulation, and exploitation of knowledge throughout the innovative process (Lichtenthaler and Ernst, 2006).

The pharmaceutical industry is, arguably, the leading industry in which markets for technology have rapidly grown and are actively utilized (Arora and Gambardella, 2010). This paper examines how R&D portfolios of pharmaceutical firms affect licensing decisions, controlling firm size, therapeutic diversity, and the degree of competition in R&D as well as product markets. The R&D portfolio of a pharmaceutical firm is mainly reflected in *drug pipelines* that consist of drug candidates under clinical testing as well as approved drugs being marketed[1]. Luckily, drug pipelines can be observed quite accurately owing to the rigorous regulatory process of clinical testing: pre-clinical, phase I, phase II, phase III, and post marketing surveillance (PMS). Accordingly, the pharmaceutical industry is a suitable candidate for examining the effect of R&D portfolios on licensing.

Licensing can be a possible way of smoothing out the state of drug pipelines across stages. The change of drug pipelines would dictate a licensing decision as a result of the portfolio adjustment process. We will refer to this causality as a *portfolio effect*. For example, a firm with relatively richer drug candidates at one stage than at other stages will be likely to license some of the drug candidates outward at that stage. In contrast, if the number of drug candidates at a stage is diminishing compared to other stages, inward

[1] The present paper could not utilize detailed data on project-based R&D expenditures. Although pharmaceutical patents are frequently used in empirical studies, they mainly reflect upstream drug discovery research. The state of drug pipelines, however, can be regarded as a useful proxy for the portfolio of pharmaceutical R&D, because resource allocation among pharmaceutical research projects within a firm would be at least partly reflected in the distribution of drug candidates across therapeutic categories.

licensing at that stage would be accelerated to level off the drug pipelines across the stages.

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

However, very few empirical studies in the literature explore the influence of R&D portfolios on inward or outward licensing, except for the technology transaction through mergers and acquisitions (M&A). Higgins and Rodriguez (2006) suggested that the bleak prospect of drug pipelines induced M&A between U.S. pharmaceutical companies. Using data on 160 pharmaceutical firms' acquisitions from 1994 to 2001, they defined the *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 by using M&A data of 383 pharmaceutical firms from 1988 to 2001.

Most previous studies focused on complementary assets as a significant determinant of licensing (Teece, 1986; Montalvo and Yafeh, 1994; Arora et al., 2001a, 2001b; Shane, 2001; Kollmer and Dowling, 2004; Arora and Ceccagnoli, 2006; Fosfuri, 2006; Gambardella et al., 2007). That is, a firm with complementary assets would absorb knowledge more effectively and exploit profit opportunities more efficiently, thereby exploiting its own inventions internally rather than acquiring royalties by licensing them out.

As the theoretical literature points out, there are two conflicting effects with which a licensor's profit varies and the incentives to license change accordingly (Arora and Fosfuri, 2003). One is the *revenue effect*, which enhances a licensor's profit with royalties paid by licensees, and the other is the *rent dissipation effect*, which erodes a licensor's profit by intensifying competition due to a licensee's entry into the licensor's

market. Therefore, the more competition at the R&D and marketing stages, the higher the incentive to license to horizontal rivals. This is because the revenue effect outweighs the rent dissipation effect. That is, firms faced with severe competition are marginally exposed to a small rent dissipation effect by licensing their technologies out to rivals, and they can obtain large royalty revenues through licensing because there are many potential licensees. We will consider the competition effect on licensing, reflecting the two conflicting strategic effects.

The data that we collected through *Asuno Shinyaku* (the comprehensive database of drug developments and alliances of Japanese pharmaceutical firms) comprises 329 license-outs and 434 license-ins closed by 54 Japanese pharmaceutical companies between 1997 and 2007 with various types of counterparts such as horizontal rivals and bio-ventures. We will define a portfolio of drug pipelines and classify the process of drug innovation into an early stage and a late stage. Thus, we will pay special attention to the stage-specific determinants of licensing, which are not fully explored in the literature.

We assume that downstream complementary assets (such as statisticians, collaborative networks with physicians, and medical representatives) and the therapeutic diversity of existent drug pipelines are *determined* prior to licensing decisions. Then, we consider that drug pipelines are *endogenously* determined, because inward and outward licensing will result in different configurations of drug pipelines. That is, drug pipelines influencing a firm's license decision are themselves influenced by a firm's license activity.

Estimates from the fixed-effect Generalized Method of Moment (GMM) model controlling endogeneity, using lagged variables as instruments, reveal that drug pipelines significantly affect stage-specific licensing. In particular, the Japanese pharmaceutical companies level off the state of drug pipelines by license-outs at the early stage and by license-ins at the late stage. That is, the number of drug candidates at the early stage is positively associated with license-outs (license-ins) at the early stage (late stage). On the other hand, the number of drug candidates at the late stage is negatively correlated with license-outs (license-ins) at the early stage (late stage).

Furthermore, we find that a pharmaceutical firm with larger sales is more likely to introduce external drug candidates at the late stage. Therefore, downstream complementary assets, which are construed as absorptive capacity, strengthen the

propensity to license-in. In contrast, the extent of R&D competition enhances the propensity to license-out, presumably due to a marginally small rent dissipation effect.

This paper is organized as follows. Section 2 explains our classification of licensing stages and the definitions of drug pipelines. It also gives an overview of pharmaceutical licensing in Japan. Section 3 presents the theoretical and empirical background of the portfolio effect and other factors affecting licensing decisions. Section 4 describes the data sources, empirical specifications, and variable constructions. Section 5 presents the estimation results. Section 6 concludes the paper.

2. Drug pipelines and pharmaceutical licensing in Japan

2.1. Drug pipelines and licensing stages

New drug development is a sequential process. The upper part of Figure 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[2]. 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). A pharmaceutical firm will submit 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 the reimbursement price. Finally, a marketed drug

[2] 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.

is subject to post marketing surveillance (PMS).

[Insert Figure 1 around here]

We divided the drug innovation process into the *early stage* and *late stage*, as shown in the lower part of Figure 1. Specifically, following Higgins and Rodriguez (2006), the early stage comprised the pre-clinical phase and phase I, and the late stage comprised all the stages after phase I.[3] We accordingly categorized drug candidates and licensing contracts by the two stages. Note that there are mainly three practical reasons for this classification[4]. First, clinical testing at the late stage (i.e., phase II and phase III) requires much higher costs than at the early stage (i.e., pre-clinical and phase I). Second, there is a fast-truck clinical testing procedure applied for life-threatening or highly effective drug candidates such as anti-cancer drugs and orphan drugs. This procedure rendered classification of drug candidates between phase II and phase III quite obscure and virtually impossible. Finally, the transition probability of clinical testing from phase I to phase II is much lower than the success rates of subsequent stages (DiMasi et al., 2003). This distinction between the early stage and the late stage helps to clarify a significant strategic effect of drug pipelines on licensing.

2.2. Stage-specific pharmaceutical licensing by firm size

Table 1 presents the stage-specific licensing activities of 54 Japanese pharmaceutical firms for the years 1997 to 2007. The calculated values represent the annual average number of licenses per firm. Table 1 classifies the number of license-ins and license-outs by firm size measured by drug sales: (i) large firms (sales $\geqq$400 billion yen), (ii) medium firms (400 $>$ sales $>$ 100), and (iii) small firms (100 $\geqq$ sales). This table shows that a large firm is likely to close a license-in contract. The annual average license-ins per firm is much higher in large firms (2.19) than in medium firms (0.74) and small firms (0.62). The bigger the firm size, the more license-ins contracts are closed at any stage (although the

[3] 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.

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

standard deviations are quite large). On the other hand, there is no significant correlation between firm size and license-outs.

[Insert Table 1 around here]

2.3. Pharmaceutical licensing by domestic and foreign partners

Figure 2 presents the trends of pharmaceutical licensing by Japanese pharmaceutical firms with foreign and domestic partners from 1997 to 2007. There are three points worth noting. First, the number of license-ins and license-outs moved roughly in parallel, although the numbers for licensing with domestic partners fluctuated more widely than those for licensing with foreign partners. Second, inward licensing always exceeds outward licensing, probably because there are many foreign and domestic licensors such as bio-ventures, universities, and foreign pharmaceutical firms. Third, the number of license-ins between 2000 and 2002 is slightly large. Slow introduction of molecular biology in the late 1990s in Japan (Henderson et al. 1999) and the introduction of biotechnologies in the early 2000s by the Japanese pharmaceutical firms (Motohashi, 2007) possibly reflect the active license-ins during this period[5].

[Insert Figure 2 around here]

3. Factors affecting licensing decisions

3.1. Portfolio effect

It is crucial for a pharmaceutical firm to keep a well-balanced portfolio, since releasing new drugs continuously secures stable cash flow and facilitates efficient use of complementary assets. Licensing can be a possible means of smoothing the state of drug

[5] In addition, the Japanese government enacted the Technology Licensing Office (TLO) Act in 1998 and the Japanese Bayh-Dole Act in 1999 to promote industry-university collaboration. These policy changes facilitated the Japanese pharmaceutical firms to contract collaborative research with universities and other public research institutes (Okada et al. 2009). Moreover, recent trends enforcing stronger intellectual property rights may reduce uncertainty and information asymmetry concerning licensing contracts (Gans et al., 2008; Lichtenthaler, 2010).

pipelines across stages. Optimal portfolios of drug candidates depend upon the combination of transition probabilities of clinical tests that are not directly observable. Given the combination of transition probabilities, the change of drug pipelines would dictate a licensing decision as a result of the portfolio adjustment process. We will hereafter refer to this causality as a *portfolio effect*. For example, a firm with relatively richer drug candidates at a stage compared with other stages given the transition probabilities constant would tend to license-out some of its drug candidates at that stage. On the other hand, if the number of drug candidates at a stage is diminishing compared to other stages, inward licensing at that stage would be promoted to level off the drug pipelines across stages.

3.2. Measuring the change of drug pipelines

As we will define fully in the subsequent section, we use three types of measures of drug pipelines: (i) the aggregate number of drug candidates across stages, (ii) the stage-specific number of drug candidates, and (iii) the relative numbers of drug candidates between adjacent stages. The basic ideas of the first and the second measures are relatively straightforward. Higher innovative performance would be reflected by the larger number of drug candidates.

By contrast, the third measure would be associated with relative innovative performance across stages. The innovative performance of the early stage relative to the drug discovery stage can be measured by the number of drug candidates at the early stage divided by research expenditures at the drug discovery stage. Unfortunately, research expenditures as well as the number of drug seeds at the drug discovery stage were not available to the present study. Therefore, we used patent stocks as the denominator.

Concerning the relative productivity between the early and late stages, if success probabilities of clinical testing (which are basically determined by firm-specific capabilities and institutional factors) are not virtually changed, the optimal structure of the drug pipelines will be stable and the innovative performance of the late stage relative to the early stage can be measured by the number of drug candidates at the late stage divided by the number of drug candidates at the early stage. If the structure of drug pipelines varies, however, licensing decisions at all stages will accordingly change depending on the portfolio effect.

Possible other sources of variation in licensing decisions are the rent dissipation effect, revenue effect, and complementary assets. These factors would accentuate or offset the portfolio effect. Particularly, we suspect that (i) the relatively stronger rent dissipation effect compared to revenue effect may offset the portfolio effect, and (ii) downstream complementary assets may raise the optimal size of drug candidates at the late stage. We will clarify these points below.

3.3. The portfolio effect on outward licensing

License-out at the early stage

If the innovative productivities at both the early stage and the late stage affect the licensing decisions at the early stage distinctively in the opposite directions, this indicates the existence of the portfolio effect, which would lead to leveling off the drug pipelines. More specifically, higher innovative performance at the early stage leads to more drug candidates at the early stage. Therefore, the growth of drug candidates at the early stage would stimulate license-outs at the early stage for smoothing drug pipelines. For a similar reason, the increase in drug candidates at the late stage would discourage outward licensing at the early stage.

License-out at the late stage

The portfolio effect on outward licensing at the late stage can be explained in a similar manner. That is, an increase of drug candidates at the late stage would stimulate license-outs at the late stage. In contrast, an increase of drug candidates at the early stage would discourage outward licensing at the late stage.

It should be noted, however, that the incentive to license-out may vary depending on the magnitude of the rent dissipation effect relative to revenue effect. Although these two effects are not distinctively observable in the present study, the rent dissipation effect at the late stage should be much larger than the one at the early stage. This is because license-outs at the late stage would intensify product market competition in the near future. Thus, the rent dissipation effect at the late stage may outweigh the revenue effect as well as the portfolio effect. In addition, the large size of downstream complementary assets possibly discourages outward licensing at the late stage. Therefore, a firm with a large number of drug candidates at the late stage may be reluctant to engage

in license-outs at that stage.

3.4. The portfolio effect on inward licensing

License-ins at the early stage

The portfolio effect will have a similar impact upon inward licensing. More specifically, the growth of drug candidates at the early stage would discourage license-ins at the early stage, whereas the increase in drug candidates at the late stage would encourage inward licensing at the early stage in order to smooth out drug pipelines across stages.

License-ins at the late stage

A firm with more drug candidates at the late stage will reduce license-ins at that stage, while a firm with fewer drug candidates at the late stage will buy external drug candidates to maintain downstream complementary assets. Therefore, the decrease in drug candidates at the late stage will result in a much higher likelihood of license-ins at the late stage.

The increase of drug candidates at the early stage would encourage inward licensing at the late stage. However, it should be noted that the complementary assets of a pharmaceutical firm are not malleable and most relevant expenditures are sunk. Therefore, a decrease of drug candidates at the early stage may not result in less inward licensing at the late stage. That is, the complementary assets may virtually predetermine the optimal size of drug candidates at the late stage: Inward licensing at the late stage may be strategically dictated by the size of the complementary assets and not by the number of drug candidates at the early stage. We will further discuss this issue in the subsequent sections.

Our predictions regarding portfolio effects on license-outs and license-ins are summarized in Table 2. The plus sign means the positive correlation between the innovative productivities of clinical testing and the likelihood of licensing at a corresponding stage, while the minus sign represents the negative one. As shown in Table 2, the portfolio effect would produce the opposite signs within a column set of explanatory variables. Furthermore, we expect explanatory variables would produce the same signs of coefficients diagonally as well as off-diagonally. Note that, however, the rent dissipation effect may outweigh the portfolio effect at the late stage. Moreover, the

presence of complementary assets would produce a strong incentive to hoard more drug candidates at the late stage of license-outs and at the early stage of license-ins.

[Insert Table 2 around here]

3.5. Control factors

Firm size

As theoretically shown by Teece (1986) and Arora and Fosfuri (2003), complementary assets may reduce the propensity to license-out. Most literature regards firm size as the proxy for complementary assets. Unfortunately, there is conflicting evidence regarding the relationship between firm size and propensity for *outward* licensing. In Japan, for example, Ohnishi and Okada (2005) and Motohashi (2008) provided evidence that larger firms less frequently closed license-outs than smaller ones[6]. On the contrary, Nakamura and Odagiri (2005) and Nagaoka and Kwon (2006) showed that larger firms were most likely to engage in license-outs[7].

With regard to the relationship between firm size and inward licensing, Cohen and Levinthal (1989, 1990) convincingly argue that large firms have a greater absorptive capacity to assimilate and exploit existing outside technologies. There is a growing body of literature which empirically supports the positive effect of absorptive capacity on license-ins (Lichtenthaler, 2009; Lichtenthaler and Lichtenthaler, 2009; Eom and Lee, 2010, among others). Thus, we expect that larger firms would maintain complementary assets at least partly by outsourcing external drug candidates.

Therapeutic Diversity

Pharmaceutical firms dealing with a large number of therapeutic fields have a better capability to assimilate external knowledge. Specifically, co-specialized assets used in R&D, manufacturing, and marketing may be an important source of scope economies

[6] Fosfuri (2006) and Arora and Ceccagnoli (2006) also obtained empirical evidence supporting the theoretical arguments by Teece (1986) and Arora and Fosfuri (2003).

[7] Gallini (1984) provided theoretical arguments supporting the positive relationship between firm size and license-outs: A dominant firm may strategically license-out its technologies in order to prevent competitors from developing better technologies. Rockett (1990) developed a similar argument, suggesting that a large firm licenses out its technologies to a weak rival in order to crowd out other stronger competitors. Furthermore, Kim (2004) suggested that a larger firm may not be worried with regard to an increase in competitors because of its dominant market position.

(Henderson and Cockburn, 1996; Cockburn and Henderson, 2001). Thus, it will become much easier for a more diversified firm to assimilate a wide range of external knowledge; therefore, a firm dealing with more diverse therapeutic fields should be more inclined to close license-ins.

To our knowledge, there are no solid theoretical predictions regarding the relationship between therapeutic diversity and outward licensing. Lichtenthaler (2010) interestingly found a positive correlation between product diversification and license-outs, but without convincing arguments. Firms with diverse therapeutic fields probably find various types of potential licensees with more ease at either the upstream or downstream innovation process.

Competitors in R&D and the product market

Arora and Fosfuri (2003) indicate that outward licensing would be inhibited to some extent due to competition in R&D and the product market, assuming all else is equal. If technologies and markets are not differentiated, it is difficult to appropriate the outcome of R&D by a single firm. In this case, the rent dissipation effect caused by an additional competitor is expected to be smaller. On the other hand, the large number of potential licensees would mean more expected royalties from licensing (i.e., a stronger revenue effect). Thus, R&D competition would raise the profitability of license-outs. Fosfuri (2006) and Kim and Vonotras (2006) obtained evidence that is consistent with this argument.

There are very few empirical studies examining the competition effect on inward licensing. In very recent studies, Allain et al. (2010) and Grimpe and Hussinger (2010) indicated that technology competition has a positive impact on the propensity to license-in. In a similar vein, Lichtenthaler (2010) found that competition fostered technology diffusion and enhanced the demand in technology markets. Therefore, the increase in competitors in R&D as well as the product market will raise the incentive to license-in as well as to license-out.

4. Empirical analysis

4.1. Data

We obtained data on 54 pharmaceutical firms that are members of the Japan Pharmaceutical Manufacturers Association (JPMA). JPMA is an industry association of research-oriented pharmaceutical manufacturers that has 68 members as of 2010. From the 68 firms, we excluded 14 firms which were 100% foreign-owned companies or whose main business lines were generic drugs, medical devices, or Chinese herbal medicines. Although foreign-owned companies have become increasingly present in the Japanese pharmaceutical market, the licensing determinants of foreign-owned companies located in Japan would most likely be different from those of the Japanese companies. Furthermore, it is very unlikely that R&D pipelines on generic drugs, medical devices, or Chinese herbal medicines are associated with the licensing decisions regarding new molecular entities (NMEs).

The complementary nature between M&A and licensing provokes concerns about endogeneity regarding licensing decisions. Fortunately, however, there were very few M&A in the Japanese pharmaceutical industry until quite recently. Hence, M&A as a missing explanatory variable would not cause very serious endogeneity issues.[8]

We used three types of data: the number of licenses, drug pipelines, and firm characteristics. Data sources for these are described as follows.

Licensing

We investigated the licensing contracts of the 54 firms through websites, financial reports, and *Asuno-Shinyaku* (Technomics, Inc.). Asuno-Shinyaku is a comprehensive database of drug developments and alliances for Japanese pharmaceutical firms. Asuno-Shinyaku collects information through various sources such as publications, news releases, and interviews. Using these data sources, we collected the data on 329 license-outs and 434 license-ins from 1997 to 2007.

[8] Horizontal M&A between major Japanese pharmaceutical companies have occurred since 2005, such as Tanabe and Mitsubishi Pharma in 2005 (the present name is Tanabe-Mitsubishi), Fujisawa and Yamanouchi in 2005 (Astellas), Dainippon and Sumitomo in 2005 (Dainippon-Sumitomo), and Daiichi and Sankyo in 2007 (Daiichi-Sankyo). Resulting changes of pipelines may provoke concerns about empirical regularities; therefore, for a robustness check we used data from 1997 to 2005 instead. We found virtually similar results for the years 1997–2007. Therefore, the present paper mainly used the larger dataset for 1997 to 2007. Regarding consolidated firms within our observation period, we collected data on firm characteristics at the time when licensing contracts were closed.

Drug pipelines

Next, the data on drug pipelines for the 54 firms were extracted from *Pharmaprojects* (Informa UK Ltd.). In addition, we divided drug candidates for the pipelines into 16 therapeutic fields using the *Anatomical Therapeutic Classification* (ATC) prepared by the European Pharmaceutical Market Research Association[9].

Firm Characteristics

Finally, we collected information about firm characteristics such as firm size and therapeutic diversity. We collected data on drug sales except for non-drug business sales from *Katsudo Gaikyo Chosa* (annual questionnaire surveys conducted by the JPMA). We also collected data on individual sales in the 16 therapeutic fields for each firm from the *IMS World Review* (IMS Health).

4.2. Empirical specifications

Our basic empirical specification is

$$(\#\text{of license at stage } s)_{\text{it}} = \sum \beta_s^k (\text{state of pipelines at stage } k)_{it} + Z\gamma + \alpha_i + \alpha_t + \varepsilon_{it}$$

where subscript i shows a firm and t represents a year. The stage s or k represents either the early or the late stage, as defined previously. The dependent variable is either the number of license-outs or license-ins. We use several dependent variables for license-outs and license-ins alternatively. Specifically, regarding license-outs, *out_total* is the total number of license-outs, and *out_early* (*out_late*) is the number of license-outs at the early stage (late stage). We define *in_total*, *in_early*, and *in_late* regarding license-ins in a similar way. β_s^k is an estimated parameter for the state of pipelines at stage k in which the corresponding dependent variable is the number of licenses at stage s. Specifically, there are four combinations of stage s and stage k in β_s^k. That is, we have four parameters of β_E^e, β_E^l, β_L^e, and β_L^l where subscript E (L) indicates the early stage of licensing (late stage of licensing) and superscript e (l) indicates the early stage of drug

[9] ATC comprises: (1) alimentary T. & metabolism, (2) blood & B. forming organs, (3) cardiovascular system, (4) dermatologicals, (5) G.U. System & sex hormones, (6) systemic hormones, (7) systemic anti-infectives, (8) hospital solutions, (9) antineoplast & immunomodul, (10) musculo-skeletal system, (11) central nervous system, (12) parasitology, (13) respiratory system, (14) sensory organs, (15) diagnostic agents, and (16) various.

pipelines (late stage of drug pipelines). Z represents the column vector of control variables, and γ is the row vector of corresponding parameters. Finally, α_i shows a fixed effect for firm i, α_t represents year dummies, and ε_{it} is an error term.

This specification raises concerns about possible endogeneity due to reverse causality: Drug pipelines influencing a firm's license are themselves influenced by the firm's licensing activity[10]. In order to cope with the endogeneity, we will use the fixed-effect GMM. GMM is an extremely general framework because an error term is not assumed to be *i.i.d*. Instrumental variables should correlate with drug pipelines but be exogenous to the dependent variable. We use both one-year and two-year lagged variables of drug pipelines as instruments because they are assuredly correlated with present drug pipelines but they are not presumably correlated with present licensing decisions. The J-test supports the validity of the instrumental variables[11].

Drug pipelines and the portfolio effect

We examine the portfolio effect on licensing by using three different specifications. As a first step, we employ regressions with either the total number of license-outs (*out_total*) or the total number of license-ins (*in_total*) as a dependent variable. The total number of drug candidates (*p_total*) is a key independent variable. That is,

$$\left.\begin{array}{c} out\_total_{\text{it}} \\ \text{or} \\ in\_total_{it} \end{array}\right\} = \beta\,(p\_total_{it}) + Z\gamma + \alpha_i + \alpha_t + \varepsilon_{it}.$$

Second, we use a stage-specific number of licensing (*out_early*, *out_late*, *in_early*, or *in_late*) as a dependent variable. Then we incorporate both the number of drug candidates at the early stage (*p_early*) and that of drug candidates at the late stage (*p_late*) as independent variables reflecting the state of pipelines. That is,

[10] According to the *Pharmaproject* data, a licensed drug candidate in a certain year is included in the drug pipeline in the same year. Therefore, this could partially offset the true negative correlation between license-ins and drug candidates in the same year.

[11] According to Kleibergen-Paap rk LM statistics (Kleibergen and Paap, 2006), the null of a weak instrument is significantly rejected. If we use three-year lagged variables as instruments, weak instruments are detected. Thus, we determined that the combination of one-year and two-year lagged variables of instruments is suitable for our estimation.

$$\left.\begin{array}{c} out\_early_{\text{it}} \\ \text{or} \\ in\_early_{\text{it}} \end{array}\right\} = \beta_E^e(p\_early_{it}) + \beta_E^l(p\_late_{it}) + Z\gamma + \alpha_i + \alpha_t + \varepsilon_{it}$$

and

$$\left.\begin{array}{c} out\_late_{\text{it}} \\ \text{or} \\ in\_late_{\text{it}} \end{array}\right\} = \beta_L^e(p\_early_{it}) + \beta_L^l(p\_late_{it}) + Z\gamma + \alpha_i + \alpha_t + \varepsilon_{it}$$

where subscript E (L) indicates that licensing occurs at the early stage (late stage); meanwhile, superscript e (l) indicates that a corresponding explanatory variable is the number of drug candidates at the early stage (late stage).

Finally, as alternative independent variables for drug pipelines, we incorporate the measures of innovative productivity, as mentioned in Section 3.2. We define the innovative productivity at the early stage as the number of drug candidates at the early stage divided by patent stocks (i.e., p_early / pat_stock)[12]. We employ a conventionally used measure of patent stock (pat_stock) as a proxy for the research expenditure at the early stage (Lach, 1995). In pharmaceutical research, a patent should be filed relatively early in the drug discovery process, probably due to low imitation costs. Therefore, patent stock can be regarded as the research input at the drug discovery stage.

Similarly, we define the state of pipelines by the number of drug candidates at the late stage divided by the number of drug candidates at the early stage (i.e., p_late / p_early). We introduce p_early / pat_stock and p_late / p_early as independent variables, and the stage-specific number of licensing (out_early, out_late, in_early, or in_late) as a dependent variable as follows:

$$\left.\begin{array}{c} out\_early_{\text{it}} \\ \text{or} \\ in\_early_{\text{it}} \end{array}\right\} = \tilde{\beta}_E^e\left(\frac{p\_early_{it}}{pat\_stock_{it}}\right) + \tilde{\beta}_E^l\left(\frac{p\_late_{it}}{p\_early_{it}}\right) + Z\gamma + \alpha_i + \alpha_t + \varepsilon_{it}$$

and

[12] We collected pharmaceutical patent applications defined by IPC: A61K. Patent stock is constructed following the conventional method in the literature. See, for example, Lach (1995). We used a 20% knowledge depreciation rate.

$$\left.\begin{array}{c} out\_late_{\text{it}} \\ \text{or} \\ in\_late_{\text{it}} \end{array}\right\} = \tilde{\beta}_L^e\left(\frac{p\_early_{it}}{pat\_stock_{it}}\right) + \tilde{\beta}_L^l\left(\frac{p\_late_{it}}{p\_early_{it}}\right) + Z\gamma + \alpha_i + \alpha_t + \varepsilon_{it}.$$

4.3. Control variables

We adopted three types of controls in regressions, firm size, therapeutic diversity, and competitors in both R&D and the product market, as mentioned in Section 3.5. We briefly describe our variable construction methods below. [13]

Firm size

Firm size can be regarded as the proxy for complementary assets. We employed drug sales (*sales*) representing a firm size. We used the Corporate Goods Price Index (GCPI, Bank of Japan) as a deflator of drug sales given 2000 as a base year.

Therapeutic diversity

We defined the therapeutic diversity index of sales (*scope*). We classified drug sales into 16 therapeutic fields according to the ATC, and calculated the Herfindahl index (*H*) based on the sales share. Then we defined the diversity index as $1/H$.

R&D and market competition

We constructed two types of competition indices either at the clinical testing stage (i.e., from pre-clinical to phase III) or at the product market stage (i.e., at the PMS stage). We constructed the competition index at the clinical stage (*comp_develop*) using the Herfindahl index weighted by the number of drug candidates. In a similar way, we defined the competition index at the product market stage (*comp_market*) by the Herfindahl index weighted by drug sales of the 16 ATC categories. Table 3 summarizes variable definitions and basic statistics.

[13] See the Appendix for more detail regarding variable constructions on therapeutic diversity as well as either R&D or market competition. In unreported regressions, we employed sales growth as an additional explanatory variable, since this could be a mitigating factor against the rent dissipation effect (see Fosfuri, 2006). However, we could not obtain any significant results on this variable. Therefore, we omitted a sales growth variable in the present study.

[Insert Table 3 around here]

5. Estimation results

We present our estimation results in the order of the three sets of empirical specifications. Note that, in the previous section, we defined three measures of drug pipelines: (i) the aggregate number of drug candidates across stages *(p_total*), (ii) the stage-specific number of drug candidates (*p_early* and *p_late*), and (iii) the relative numbers of drug candidates between adjacent stages (*p_early* / *pat_stock* and *p_late* / *p_early*). Correspondingly, we defined dependent variables as *out_total* and *in_total* for the first definition, and *out_early*, *out_late*, *in_early*, and *in_late* for the second and third definitions.

5.1. Aggregate number of drug candidates across stages

Table 4 presents the estimation results with the total number of outward licenses (*out_total*) and inward licenses (*in_total*) as dependent variables. Independent variables are the total number of drug pipelines (*p_total*), real drug sales (*sales*), therapeutic diversity (*scope*), competition indexes (*comp_develop* and *comp_market*), and year dummies (*d_year*). The variable *p_total* is regarded as endogenous, thereby the combination of one-year and two-year lagged variables is used as an instrument in fixed-effect GMM.

[Insert Table 4 around here]

The most interesting outcome of Table 4 is that the total number of drug pipelines has a significant impact on outward and inward licensing in opposite directions. That is, the coefficient of the total number of drug candidates (*p_total*) is positive for the total number of license-outs (*out_total*) at the 5% significance level, whereas it is negative for the total number of license-ins (*in_total*) at the 1% significance level[14]. The

[14] Concerns about multicollinearity between *sales* and *p_total* led us to exclude either one of these variables,

negative relationship between drug pipelines and inward licensing is consistent with the results found in Higgins and Rodriguez (2006) and Danzon et al. (2007).

Most control variables have no significant impact on licensing except for *sales* and *comp_develop*. The coefficient of *sales* is positive for the total number of inward licenses (*in_total*) at the 1% significance level. This indicates that a large firm is eager to engage in license-ins, possibly for the purpose of maintaining existent complementary assets. Competition at the development stage (*comp_develop*) has a positive impact on the total number of license-outs (*out_total*) at the 5% significance level.

5.2. Stage-specific number of drug candidates

Next, we employed the second empirical specification of stage-specific determinants of license-outs and license-ins at either the early or the late stage. Table 5 shows estimation results. The dependent variables are *out_early*, *out_late*, *in_early*, and *in_late*. We used the number of drug candidates both at the early stage (*p_early*) and at the late stage (*p_late*) as our key independent variables in this specification. Control variables are the same as the ones in Table 4.

[Insert Table 5 around here]

License-outs

Equations (1) and (2) in Table 5 present the determinants of license-outs at the early stage and late stage, respectively. First, we found that *out_early* in Eq. (1) positively correlated with *p_early* but negatively correlated with *p_late*. This combination of the opposite signs of the pipeline variables is consistent with our prediction in Table 2, indicating the presence of the portfolio effect on outward licensing at the early stage.

Next, in Eq. (2) in Table 5, the coefficient of *p_late* is negative and significant but the one for *p_early* has no significant impact on *out_late*. These results are not consistent with our prediction regarding the portfolio effect. One possible reason is that license-outs at the late stage may be subject to much a stronger rent dissipation effect than at the early stage. That is, license-outs at the late stage can induce fiercer competition in

although the estimation results showed the same signs with a virtually similar significance level as those of our basic model above.

the near future due to a much shorter gestation lag of clinical tests for the drug candidates. Another possible reason is that a firm with a large number of drug candidates at the late stage already owns large complementary assets, so that it has to maintain and efficiently use the downstream assets instead of licensing drug candidates outward.

Furthermore, from Tables 4 and 5, we obtained the positive although weakly significant relationship between the frequency of outward licensing and the degree of competition at the development stage (*comp_develop*). This indicates that, with many competing drugs at the development stage, it would be difficult to appropriate the technologies of a relevant therapeutic field from other competitors and potential licensees. Accordingly, the expected return of a drug candidate in the future would be lower. In these circumstances, the revenue effect may outweigh the rent dissipation effect so that a pharmaceutical firm will likely be more inclined to license-out drug candidates (Arora and Fosfuri, 2003).

License-ins

Equations (3) and (4) in Table 5 summarize the determinants of license-ins at the early stage and late stage, respectively. First, what we found significant was that *in_late* in Eq. (4) positively correlated with *p_early* whereas it negatively correlated with *p_late*. The combined result of the opposite signs indicates the presence of the portfolio effect on inward licensing at the late stage. Moreover, the coefficient of *sales* is significantly positive on *in_late*. This indicates that larger downstream complementary assets would facilitate inward licensing at the late stage.

With regard to *in_early* in Eq. (3) in Table 5, the coefficient of *p_early* is weakly significant and negative as expected, while the coefficient of *p_late* is not significant. Thus, although fewer drug candidates at the early stage may accelerate license-ins at the early stage, the attrition of drug candidates at the late stage rather stimulates license-ins at the late stage, as shown in Eq. (4).

5.3. Relative numbers of drug candidates between adjacent stages

For the purpose of a robustness check, we further employed the third empirical specification with relative numbers of drug candidates between two adjacent stages as alternative variables for drug pipelines. We incorporated the two innovative measures

defined in Section 3.2 as *p_early* / *pat_stock* and *p_late* / *p_early* into the third specification. Table 6 shows the estimation results.

[Insert Table 6 around here]

License-outs

Equations (1) and (2) in Table 6 present the determinants of license-outs at the early stage and late stage, respectively. First, in Eq. (1) we found that the dependent variable (*out_early*) positively correlated with the innovative performance at the early stage (*p_early* / *pat_stock*), while it negatively correlated with the innovative performance at the late stage (*p_late* / *p_early*). The combined result of the opposite signs in Eq. (1) for pipeline variables indicates the presence of the portfolio effect on license-outs at the early stage, similar to the previous specification.

Next, in Eq. (2) in Table 6, the coefficient of *p_early* / *pat_stock* is negative and significant but the coefficient of *p_late* / *p_early* has no significant impact on *out_late*. Although the negative coefficient of *p_early* / *pat_stock* is expected in Table 2, these results from Tables 5 and 6 suggest that the portfolio effect for license-outs is not significant at the late stage.

Finally, we obtained weakly significant coefficients for *comp_develop* in both Eqs. (1) and (2) in Table 6. Recall that the coefficients of *comp_develop* are also weakly significant and positive in Tables 4 and 5. Therefore, competition at the development stage possibly stimulates license-outs. A possible reason is that, as suggested before, the revenue effect outweighs the rent dissipation effect so that license-outs of drug candidates become increasingly active.

License-ins

Equations (3) and (4) in Table 6 show the determinants of license-ins at the early stage and late stage, respectively. First, *in_late* in Eq. (4) positively correlated with *p_early* / *pat_stock* , whereas it negatively correlated with *p_late* / *p_early* . The opposite correlations indicate the presence of the portfolio effect on inward licensing at the late stage. In addition, the coefficient of *sales* is significantly positive on *in_late* in the same

way in Table 5.

Concerning *in_early* in Eq. (3) in Table 6, the coefficient of *p_early* / *pat_stock* is weakly significant and negative as expected, while the coefficient of *p_late* / *p_early* is not significant. This is virtually the same as the results shown in Table 5.

In sum, we found that the Japanese pharmaceutical companies evened out drug pipelines by licensing-out at the early stage and by licensing-in at the late stage. It is safe to say that licensing is a significant means of smoothing the state of drug pipelines across stages, even though license-outs at the late stage may be influenced by the rent dissipation effect and license-ins at the late stage will be affected by complementary assets.

6. Conclusions

The present paper examined a portfolio effect, namely, how a portfolio of drug candidates affected stage-specific licensing by the Japanese pharmaceutical companies. We classified the timing of licensing and drug pipelines into an early and a late stage for the purpose of examining stage-specific incentives to license, which have not been fully explored in previous studies.

Our empirical results are summarized as follows. The state of drug pipelines significantly affected licensing decisions at the early and late stages even when we controlled for firm size, therapeutic diversity, and the degree of competition. In particular, the Japanese pharmaceutical companies leveled off drug pipelines by either license-outs at the early stage or license-ins at the late stage. That is, the number of drug candidates at the early stage positively correlated with license-outs (license-ins) at the early stage (late stage). Further, the number of drug candidates at the late stage negatively correlated with license-outs (license-ins) at the early stage (late stage). The combined results of the opposite impacts of the pipeline on licensing indicate that licensing plays a significant role in smoothing out the state of drug pipelines across stages.

In contrast, we could not find a significant impact of the portfolio effect on license-outs at the late stage. A possible reason is that the rent dissipation effect

dominates the portfolio effect at the late stage. Another possible reason is that a large number of drug candidates at the late stage would require a large size of complementary assets, so that it was preferable to maintain and efficiently use the downstream assets to license-out drug candidates. With respect to license-ins at the early stage, the exhaustion of drug candidates at the late stage stimulated license-ins at the late stage, although fewer drug candidates at the early stage accelerated license-ins at the early stage.

This paper contributes to the literature in several ways. Most previous empirical studies focused on the determinants of license-outs, mainly referring to complementary assets and revenue and/or the rent dissipation effect. The present paper, however, considered explicitly how an R&D portfolio of drug pipelines affected licensing decisions, controlling for firm size, therapeutic diversity, and competitors in R&D and product markets. Furthermore, we examined both outward and inward licensing. Thus, our analysis offers a more complete and clear picture of a firm's involvement in markets for technology.

This paper has several limitations. First, our dataset consisted of licensing contracts of drug candidates. The present study did not use information on other types of licenses, such as research tools and biotechnologies. These restrictions may underestimate the growing role of technology markets in pharmaceutical R&D.

Second, we did not consider the economic value of a licensing contract. The value of a drug candidate differs significantly according to licensing stage and potential market size. However, the changing features of option values at different stages would demand further information on therapeutically distinctive market conditions and may require a more complicated exploration strategy.

Finally, we could not introduce pairwise controls of the characteristics of licensors and licensees, as was done by Kim and Vonotras (2006), mainly due to data restrictions. This requires broader and more comprehensive data collection. It is natural to consider license-ins and license-outs to be jointly determined by a pharmaceutical firm. Therefore, it is desirable to estimate simultaneously the determinants of license-ins and license-outs. This remains to be examined in future empirical research.

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Appendix:
Variable construction on therapeutic diversity and competition indexes

Therapeutic diversity

We calculate sales share T_{ikt} in each of the 16 therapeutic fields of ATC,

$$\sum_k T_{ikt} = 1$$

where *k* represents a therapeutic field (1, 2, …, *K*), *i* is a firm (1, 2, …, *N*), and *t* denotes the year. Then, we construct the therapeutic diversity of the firm, *scope*, using the Herfindahl index of $\sum_k T_{ikt}^2 = H_{it}$, as follows.

$$scope_{it} = \frac{1}{H_{it}}.$$

The degree of competition in R&D

First, we calculate the competition index at the development stage, *comp_develop*, as follows. We calculate the share of drug candidates across firms, X_{ikt}, in each of the 16 therapeutic fields of ATC.

$$\sum_i X_{ikt} = 1$$

where *k* represents a therapeutic field (1, 2, …, *K*), *i* is a firm (1, 2, …, *N*), and *t* denotes the year. Thereafter, we create the diversity index C_{kt} in each therapeutic field through the Herfindahl index $\sum_i X_{ikt}^2 = A_{kt}$, that is,

$$C_{kt} = \frac{1}{A_{kt}}.$$

Finally, we obtain the competition index in R&D, *comp_develop*, based on X_{ikt} and C_{kt} as follows:

$$comp\_develop_{it} = \sum_k X_{ikt} C_{kt}.$$

The degree of competition in product market

Next, we calculate sales share S_{ikt} in each of the 16 therapeutic fields of ATC.

$$\sum_i S_{ikt} = 1$$

where *k* represents a therapeutic field (1, 2, …, *K*), *i* is a firm (1, 2, …, *N*), and *t* denotes the year. Thereafter, we create the diversity index D_{kt} in each therapeutic field through the Herfindahl index $\sum_i S_{ikt}^2 = B_{kt}$, that is,

$$D_{kt} = \frac{1}{B_{kt}}.$$

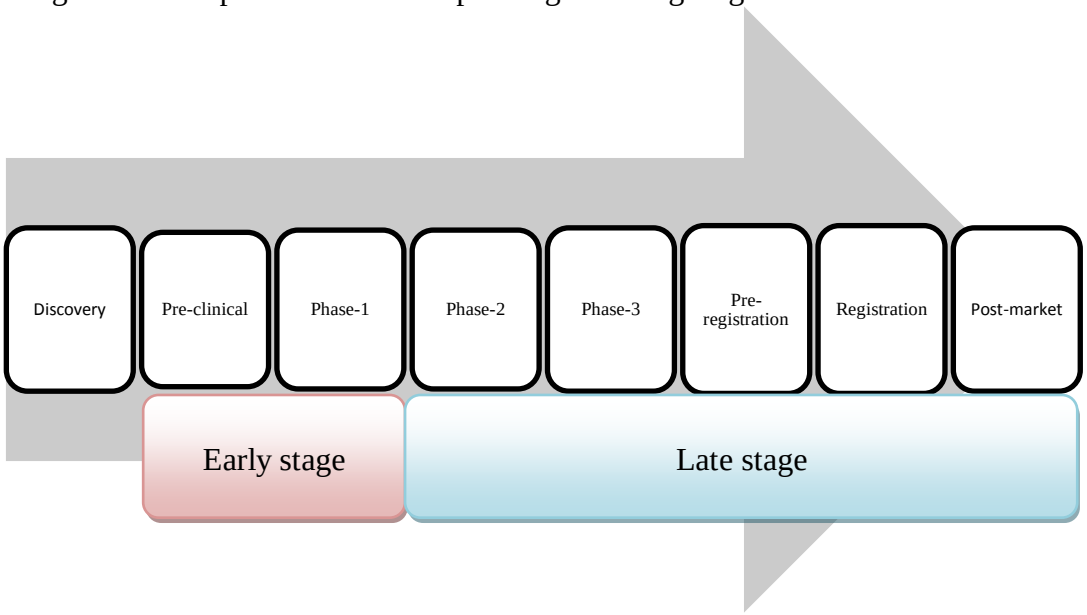
Finally, we obtain the competition index in the product market, *comp_market*, based on S_{ikt} and D_{kt} as follows:

$$comp\_market_{it} = \sum_k S_{ikt} D_{kt}.$$

Thus, the competition index of *comp_market* is defined using the Herfindahl index B_{kt} weighted by drug sales S_{ikt} in 16 ATC therapeutic markets.

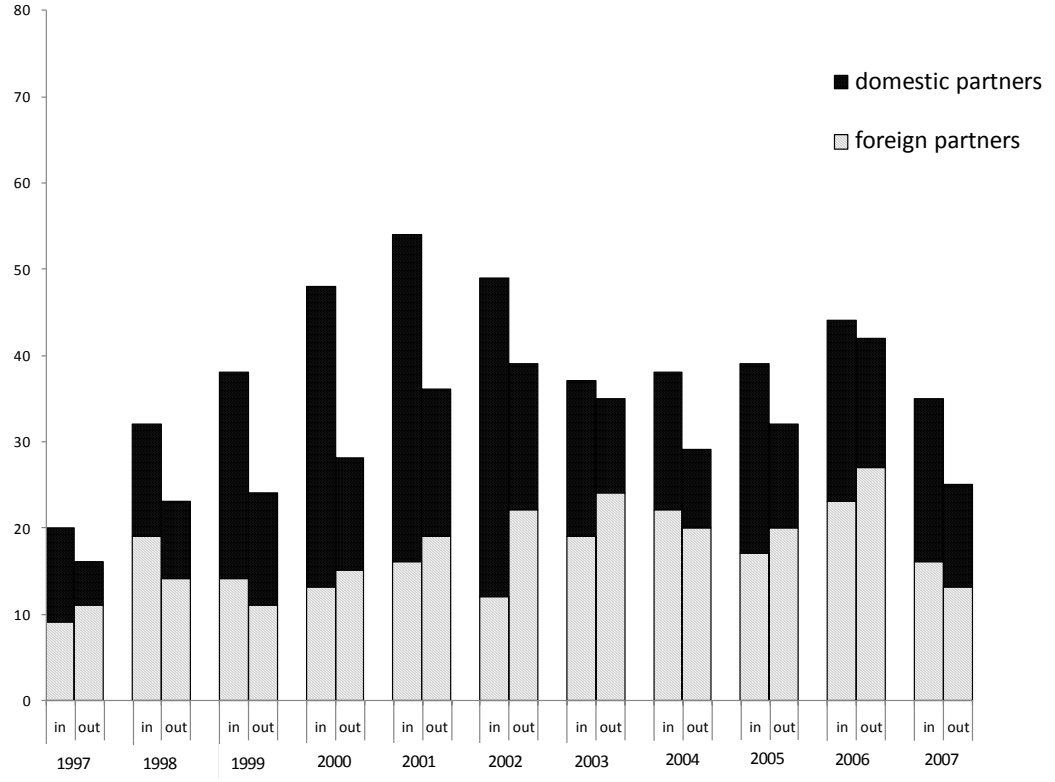
Figures and Tables

Figure 1
Drug innovation process and corresponding licensing stages



Note: The upper part of the figure shows the innovation process from drug discovery to post-market surveillance. The lower part of the figure depicts the authors' classification of drug pipelines. See the text for more detail.

Figure 2
Number of licenses with foreign and domestic partners by pharmaceutical firms in Japan



Total number	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	Total
License-ins	20	32	38	48	54	49	37	38	39	44	35	434
License-outs	16	23	24	28	36	39	35	29	32	42	25	329

Data source: *Asuno Shinyaku*, Technomics, Inc.

Table 1
Stage-specific licensing: Annual average number of licenses per firm from 1997 to 2007

Firm size (billion yen)	Number of firms	License-ins			License-outs		
		Total	Early stage	Late stage	Total	Early stage	Late stage
Large sales≧400	8	2.19 (1.79)	0.85 (0.98)	1.35 (0.64)	0.79 (1.10)	0.24 (0.55)	0.55 (0.33)
Medium 400＞sales＞100	14	0.74 (0.82)	0.37 (0.59)	0.37 (0.34)	0.88 (1.07)	0.40 (0.63)	0.48 (0.42)
Small 100≧sales	32	0.62 (0.92)	0.29 (0.62)	0.33 (0.32)	0.50 (0.88)	0.23 (0.53)	0.27 (0.35)
Total	54	0.83 (1.14)	0.38 (0.69)	0.46 (0.39)	0.63 (0.98)	0.27 (0.56)	0.35 (0.37)

Note: Standard deviations are given in parentheses.
Data source: *Asuno Shinyaku*, Technomics, Inc.

Table 2
Portfolio effect on license-out and license-in

	License-out		License-in	
	Early stage	Late stage	Early stage	Late stage
Innovative productivity at the early stage	+	−	−	+(?)
Innovative productivity at the late stage	−	+(?)	+	−

Table 3
Definition and basic statistics of variables (units: 54 firms, year: 1997–2007)

Variable	Definition	Obs	Mean	Std. Dev.	Min	Max
License-outs	Number of outward licensing					
out_total	Total number	524	0.63	0.94	0	5
out_early	Early stage	524	0.27	0.57	0	3
out_late	Late stage	524	0.35	0.68	0	4
License-ins	Number of inward licensing					
in_total	Total number	524	0.83	1.14	0	8
in_early	Early stage	524	0.38	0.69	0	5
in_late	Late stage	524	0.46	0.80	0	5
R&D Pipeline						
p_total	Total number of drug pipelines	524	28.65	24.24	0	165
p_early	Drug pipelines at the early stage	524	5.75	5.71	0	36
p_late	Drug pipelines at the late stage	524	22.90	19.92	0	133
pat_stock	Patent stock (20% depreciation rate)	513	83.00	99.78	0	632.56
p_early / pat_stock	*p_early* divided by *pat_stock*	506	0.13	0.12	0.01	1.33
p_late / p_early	*p_late* divided by *p_early*	524	4.05	3.17	0	26
Controls						
sales	Real drug sales (hundred billion yen in 2000)	501	1.48	2.12	0.02	15.09
scope	Therapeutic diversity index in drug sales	491	3.32	1.51	1.00	7.73
comp_develop	Competition index at the development stage	504	15.28	4.09	4.71	27.97
comp_market	Competition index at the product market	491	17.58	4.07	5.37	29.38

Note 1: See section 2.1 for the division of licensing and pipeline stages.
Note 2: See section 4.3 and the Appendix for the detailed definition of therapeutic diversity and competition indexes.

Table 4
Estimation result of aggregate number of drug candidates across stages

	out_total	***in_total***
R&D Pipeline		
p_total	0.012** (0.006)	−0.078*** (0.029)
Controls		
sales	−0.100 (0.062)	0.826*** (0.221)
scope	0.083 (0.054)	0.181 (0.199)
comp_develop	0.060** (0.029)	−0.051 (0.045)
comp_market	0.053 (0.055)	−0.347 (0.265)
d_year	yes	yes
Number of observations	359	359
Number of groups	47	47
Hansen J statistics	0.363 (p = 0.547)	1.248 (p = 0.264)

Note 1: *** 1%, ** 5%
2: Robust standard errors are given in parentheses.
3: Instrumented: *p_total*. Instruments: One- and two-year lagged *p_total*.

Table 5
Estimation results of stage-specific number of drug candidates

	License-outs		License-ins	
	(1)	(2)	(3)	(4)
	out_early	***out_late***	***in_early***	***in_late***
R&D Pipeline				
p_early	0.092***	0.048	−0.058*	0.100***
	(0.034)	(0.031)	(0.036)	(0.036)
p_late	−0.049*	−0.071**	−0.030	−0.081***
	(0.029)	(0.033)	(0.028)	(0.030)
Controls				
sales	0.099	0.227	0.215	0.661***
	(0.152)	(0.138)	(0.182)	(0.201)
scope	0.153*	0.138	0.014	0.193*
	(0.089)	(0.116)	(0.097)	(0.117)
comp_develop	0.021*	0.024*	−0.003	−0.021
	(0.013)	(0.015)	(0.027)	(0.037)
comp_market	0.011	−0.014	−0.121	−0.087
	(0.056)	(0.067)	(0.101)	(0.090)
d_year	yes	yes	yes	yes
Number of observations	359	359	359	359
Number of groups	47	47	47	47
Hansen J statistics	1.922	0.210	2.437	0.861
	(p = 0.369)	(p = 0.900)	(p = 0.295)	(p = 0.650)

Note 1: *** 1%, ** 5%, * 10%.
2: Robust standard errors are given in parentheses.
3: Instrumented: *p_early* and *p_late*. Instruments: One- and two-year lagged *p_early* and *p_late*.

Table 6
Estimation results of relative numbers of drug candidates between adjacent stages

	License-outs		License-ins	
	(1)	(2)	(3)	(4)
	out_early	***out_late***	***in_early***	***in_late***
R&D Pipeline				
p_early / pat_stock	2.729**	−2.437*	−2.648*	3.037**
	(0.136)	(1.400)	(1.566)	(1.524)
p_late / p_early	−0.068**	−0.070	−0.025	−0.099**
	(0.032)	(0.056)	(0.046)	(0.040)
Controls				
sales	0.001	0.004	0.023	0.440***
	(0.066)	(0.076)	(0.176)	(0.171)
scope	0.080	0.142	0.076	0.152
	(0.106)	(0.128)	(0.120)	(0.118)
comp_develop	0.034*	0.035*	0.006	−0.016
	(0.020)	(0.020)	(0.032)	(0.036)
comp_market	−0.046	−0.013	−0.076	−0.143
	(0.063)	(0.079)	(0.093)	(0.109)
d_year	yes	yes	yes	yes
Number of observations	350	350	350	350
Number of groups	46	46	46	46
Hansen J statistics	2.577	3.803	2.264	1.286
	(p = 0.275)	(p = 0.163)	(p = 0.322)	(p = 0.525)

Note 1: *** 1%, ** 5%, * 10%.
2: Robust standard errors are given in parentheses.
3: Instrumented: *p_early* / *pat_stock* and *p_late* / *p_early*. Instruments: One- and two-year lagged *p_early* / *pat_stock* and *p_late* / *p_early*.