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Impact of Research and Development Strategy on Sustainable Growth in Multinational Pharmaceutical Companies

Fumio Teramae [1,2,*], Tomohiro Makino [1], Yeongjoo Lim [3], Shintaro Sengoku [4] and Kota Kodama [1,5,*]

1 Graduate School of Technology Management, Ritsumeikan University, Osaka 567-8570, Japan; makino.tomohiro@gmail.com
2 Eli Lilly Japan K.K., Hyogo 651-0086, Japan
3 Faculty of Business Administration, Ritsumeikan University, Osaka 567-8570, Japan; lim40@fc.ritsumei.ac.jp
4 School of Environment and Society, Tokyo Institute of Technology, Tokyo 152-8550, Japan; sengoku.s.aa@m.titech.ac.jp
5 Center for Research and Education on Drug Discovery, The Graduate School of Pharmaceutical Sciences in Hokkaido University, Hokkaido 060-0808, Japan
* Correspondence: gr0434fx@ed.ritsumei.ac.jp (F.T.); kkodama@fc.ritsumei.ac.jp or kota.kodama@cris.hokudai.ac.jp (K.K.)

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Abstract: Research and development (R&D) productivity is continuously declining, and it is said that the conventional model of pharmaceutical business is becoming obsolete. Many research studies on R&D productivity focus on inputs (e.g., strategic transactions to absorb external innovation, R&D expenditures), outputs (e.g., approvals of a new drug), and outcomes (e.g., total sales, incomes). However, few prior studies address the relationship among these three components simultaneously. Therefore, we comprehensively analyzed factors affecting R&D productivity by statistically examining a sample of 30 large multinational companies. Our results show that strategic transactions do not increase the number of approved drugs and negatively affect growth in terms of total sales. Additionally, our results show that a home-region-oriented international strategy positively affects total sales, thus indicating that responsiveness to local medical needs is important for sustainable growth. This paper contributes to the body of research on R&D productivity in the pharmaceutical industry.

Keywords: pharmaceutical industry; R&D; strategic transactions; R&D expenditures; international strategy; strategy implementation; comparison results

1. Introduction

The business activities of the pharmaceutical industry are composed of several elements: research and development (R&D), regulatory submission and launch, sales and marketing (S&M), and investment collection and reinvestment [1]. To maintain sustainable growth, pharmaceutical companies must increase income (i.e., total sales) through a continuous delivery of new products (e.g., new drugs) and optimize expenditures (e.g., R&D expenditures, S&M expenditures) through increased productivity. Although this idea applies to other industries as well, there are major differences between these other industries and the pharmaceutical sector.

One major difference is that pharmaceutical companies must obtain the official approval of the regulatory authorities of each country before a drug is placed on the market. In principle, approval is only obtained after conducting clinical trials that meet very strict regulatory requirements. As a result, the success rate from drug discovery to drug launch is very low (only 4%), and the R&D period takes an

average of 14 years. Out of these 14 years, clinical trials take an average of seven years for completion, and their costs represent 63% of the overall expenditures per new drug [2]. As regulatory requirements to ensure safety and efficacy become more stringent, the success rates of clinical trials decline [3–6], and the R&D expenditures per approved drug increase [7]. Therefore, the continuous delivery of new products in the pharmaceutical industry is more challenging compared to other industries.

Another unique aspect of the pharmaceutical industry is that the government, its related organizations, and health insurers intervene in the pricing and reimbursement of new products in countries such as England, Sweden, Canada, Australia, and Japan. These processes occur because drug costs affect healthcare financing [8,9]. The pressure on the profitability of the pharmaceutical industry is growing as healthcare budgets and expenditures increase for a rapidly aging society, especially among developed countries. Additionally, the price of a drug tends to decline after its patent expires and generic drugs are launched [10]. Meanwhile, scientifically novel and innovative drugs that satisfy unmet medical needs can generate higher profits or gain a larger market share even in this environment [11,12]. Therefore, the pharmaceutical industry requires innovation more than other industries.

To overcome these industry-specific challenges, pharmaceutical companies have become more discovery-oriented and science-driven organizations [13]. For example, some pharmaceutical companies are increasingly outsourcing research to external research organizations [14], while others are actively capitalizing on external science and research-based innovation through strategic transactions. These transactions, which include mergers and acquisitions (M&A) and R&D in-licensing, help firms acquire the newest scientific and medical knowledge on the targeted diseases, as well as cutting-edge technologies for R&D [15–17]. Actually, some of the biggest deals in terms of transaction size were announced or completed in 2019. These deals include the following: Bristol-Myers Squibb and Celgene (74 billion USD), AbbVie and Allergan (63 billion USD), Takeda and Shire (58.6 billion USD), Pfizer and Array Biopharma (11.4 billion USD), Novartis and Medicines Company (9.7 billion USD), Eli Lilly and Loxo Oncology (8 billion USD), and GlaxoSmithKline and Tesaro (5.1 billion USD).

This movement involves two aspects: one is the model of innovation process in science and another is the innovation capability-building strategy. The shift to discovery-oriented and science-driven organizations is based on the belief that the traditional linear model would work in the scientific filed. This is the basic science used to create sophisticated technologies, with economic significance. However, in recent years, the linear model has been challenged by empirical research, and new models have been proposed. One of them is the chain-linked model, based on the conviction that the basic science should be based on the customers' needs in the potential market and that the feedback loops accumulate scientific knowledge and refine technologies required for innovation. Another is the multi-channel interactive learning model, according to which the multi-channeling interface accelerates feedback loops, and the openness and agility create a competitive advantage [18]. Taking into account the uniqueness of the pharmaceutical industry mentioned above, it is unlikely that feedback loops can be used in the clinical development phase, as proposed by the chain-linked model and multi-channel interactive learning model. However, it is expected that R&D based on medical needs in the potential market will add more value according to our previous finding that the difference in international strategies reflecting the responsiveness leads to the difference in adjusted total sales [19]. To the best of our knowledge, there are only a few studies in this regard.

M&A and R&D in-licensing (i.e., technology import) is one of the innovation capability-building strategies, and the newest scientific and medical knowledge and cutting-edge technologies are examples of innovation capabilities [20]. The innovation capability-building strategies assume that pharmaceutical companies can successfully complete integration, but there are some challenges, as integration is a key goal of M&A [21]. For instance, differences in company cultures in both parties of M&A hinder the integration of all operations on both sides [22,23]. According to the classical location theory, geographical distance limits the effectiveness of knowledge transfer [24]. Time difference between R&D bases limits the effectiveness of knowledge transfer [25]. Research studies associated

with innovation processes and innovation models such as open innovation in the pharmaceutical industry are becoming more prevalent [26–28]. Despite an increase in the number of studies regarding innovation, studies on whether the absorption of innovation within the pharmaceutical industry improves R&D productivity at the enterprise level are limited. Additionally, there are conflicting results, since some studies show an overall positive impact [29,30] while other studies show a negative impact [31,32]. Moreover, according to prior research studies [2,29–32], R&D productivity must encompass three components: inputs (e.g., R&D investments), outputs (e.g., new drug launches), and outcomes (e.g., sales). Unfortunately, the number of comprehensive research studies that address these components is limited [33]. Therefore, it is still worthwhile to holistically evaluate how the R&D strategy contributes to R&D productivity at the enterprise level for sustainable growth in the pharmaceutical industry.

2. Materials and Methods

2.1. Data

In this paper, we defined a multinational pharmaceutical company as a company whose sales in foreign countries represent 10% or more of its total sales [34,35]. We regarded the increase of total sales as sustainable growth, for the sake of simplification, although sustainable growth was originally defined as the annual percentage of increase in sales that is consistent with the company's financial target [36]. We think that the growth of total sales (i.e., top line) will lead to a proactive investment in R&D.

Out of the 50 largest multinational pharmaceutical companies based on worldwide drug sales from 2010 to 2017, we analyzed 30 pharmaceutical companies (Table 1) [37,38]. We hand-collected data on M&A and R&D in-licensing for the number of strategic transactions, the R&D expenditures, the number of drugs approved by the U.S. Food and Drug Administration (FDA), the total sales, and the geographic sales from 2010 to 2017. The data sources about the strategic transactions were Crunchbase [39] and Biomedtracker [40]. We excluded the financing and marketing in-licensing transactions because their main purpose is not to absorb innovation. R&D expenditures, total sales, and geographic sales were obtained from the annual reports and financial reports such as 10-K and 20-F forms per company. We counted the sales of pharmaceutical drugs for humans and excluded the sales of drugs for animals, diagnostics, devices, and royalties as much as possible. We converted the currency units to USD based on the period average data in the International Monetary Fund's International Financial Statistics [41]. We conservatively used cumulative R&D expenditures over eight years considering the average duration of clinical trials [2] and prior research [33,42]. FDA-approved drugs were obtained from the New Molecular Entity (NME) Drug and New Biologic Approvals lists [43] because almost all the new drugs are launched in the U.S. due to the rapid internationalization of the pharmaceutical industry. The expectation of growing sales with overseas expansions occurs due to the possibility of multinational clinical trials, and a large number of clinical trials occur in the U.S. [44–46].

Multinational pharmaceutical companies are adopting a different international strategy at the enterprise level, along with other companies in other industries [19,47], which directly affects the change in total sales and R&D productivity. Using data from 2017, we classified the 30 companies into four types as per the classification established by Rugman and Verbeke [47]. Their classification was based on the concept of triad power, and the triad was a geographic space comprising the U.S., the EU, and Japan. Today, however, the triad has expanded to include North America, Europe, Asia-Pacific, and others. As of 2014, the distribution of geographic sales was roughly 40% in North America, 30% in Europe, and 30% in the Asia-Pacific region and others [17]. As the market size of the three regions is almost the same, this classification is applicable to the pharmaceutical industry, and we did not adjust the total sales by geographic sales. We noted that the geographical category of each company

could vary to some extent, because the information of European countries is not always detailed in the annual and financial reports.

Table 1. List of sample pharmaceutical companies.

Company	Home Region	Internationalization [1]
AbbVie	North America	Home-region-oriented
Alexion	North America	Global
Amgen	North America	Home-region-oriented
Astellas Pharma	Asia-Pacific/Others	Global
AstraZeneca	Europe	Global
Bayer	Europe	Global
Biogen	North America	Home-region-oriented
Boehringer Ingelheim	Europe	Global
Bristol-Myers Squibb	North America	Home-region-oriented
Celgene	North America	Home-region-oriented
Daiichi Sankyo	Asia-Pacific/Others	Home-region-oriented
Eisai	Asia-Pacific/Others	Home-region-oriented
Eli Lilly	North America	Home-region-oriented
Gilead Sciences	North America	Home-region-oriented
GlaxoSmithKline	Europe	Global
Johnson & Johnson	North America	Home-region-oriented
Merck & Co	North America	Global
Merck KGaA	Europe	Global
Mylan	North America	Global
Novartis	Europe	Global
Novo Nordisk	Europe	Host-region-oriented
Pfizer	North America	Bi-regional
Roche	Europe	Global
Sanofi	Europe	Global
Shionogi	Asia-Pacific/Others	Bi-regional
Shire	Europe	Host-region-oriented
Sumitomo Dainippon	Asia-Pacific/Others	Host-region-oriented
Takeda	Asia-Pacific/Others	Bi-regional
Teva Pharmaceutical	Asia-Pacific/Others	Host-region-oriented
UCB	Europe	Bi-regional

[1] Internationalization: Global, more than 20% of sales in all three regions; bi-regional, more than 20% of sales in two regions but less than 50% in the home region; home-region-oriented, more than 50% of sales within the home region; host-region-oriented, more than 50% of sales in one region besides the home region [47].

2.2. Analysis

For the purpose of R&D productivity, we defined the strategic transactions and the R&D expenditures as inputs, the number of approved drugs as outputs, and the change in total sales as outcomes. First, we investigated the trends in strategic transactions and R&D productivity in the pharmaceutical industry. To analyze the number of strategic transactions over time, we performed the Kruskal–Wallis test, rather than the Jonckheere–Terpstra test, because we did not expect an increase or decrease in the number of strategic transactions in advance. We used Pearson's correlation analysis to determine the relationships between individual components of R&D productivity.

Second, we compared pharmaceutical companies that are pursuing different international strategies in terms of R&D productivity to identify the possible factors that influence their productivity. We used the Shapiro–Wilk test to test for normality. If the data showed normality, we performed the Student's *t*-test or Welch's *t*-test, depending on the equivariance determined using the Levene test. If the data did not show normality, we performed the Mann–Whitney U test. We performed a multiple linear regression analysis to understand how individual components of the R&D productivity influence the output and outcome. For the type of international strategy, we created a dummy variable with 0 for global and 1 for home-region-oriented. We explored the reason why the identified possible

factors impacted R&D productivity. We performed Fisher's exact test or the Pearson Chi-Squared (χ^2) test to analyze the differences between these groups.

All statistical calculations for this study were performed in the IBM SPSS statistical software version 26.0 for Windows. A two-sided p-value < 0.05 indicates statistical significance.

3. Results

3.1. Trends in Strategic Transactions and R&D Productivity within the Pharmaceutical Industry

Figure 1a shows the trends in strategic transactions from 2010 to 2017. There is no clear trend regarding the change in the number of strategic transactions over the eight-year period (p = 0.429, Kruskal–Wallis test). Figure 1b,c show the relationship between inputs and outputs for eight years. While there is no correlation between the number of strategic transactions and the number of approved drugs (r = 0.072, p = 0.352), there is a positive correlation between the eight-year cumulative R&D expenditures and the number of approved drugs (r = 0.406, $p < 0.05$). Figure 1d shows the relationship between outputs and outcomes for eight years. There is no correlation between the number of approved drugs and the change in total sales (r = 0.015, p = 0.468). Figure 1e,f show the relationship between inputs and outcomes for eight years. While there is no correlation between the number of strategic transactions and the change in total sales (r = −0.223, p = 0.118), there is a negative correlation between the eight-year cumulative R&D expenditures and the change in total sales (r = −0.320, $p < 0.05$).

We observed that the 30 large companies have constantly absorbed external innovation by leveraging M&A rather than R&D in-licensing. However, our results indicate that the absorption of external innovation did not increase R&D productivity (i.e., no impact on outputs and outcomes). Interestingly, the cumulative R&D expenditures contributed to the advancement of clinical trials and the number of approved drugs. However, cumulative R&D expenditures did not contribute to the change in total sales. Moreover, the number of approved drugs did not contribute to the change in total sales, which implies that the indication of approved drugs might be more important for maintaining sustainable growth than the number of new drugs.

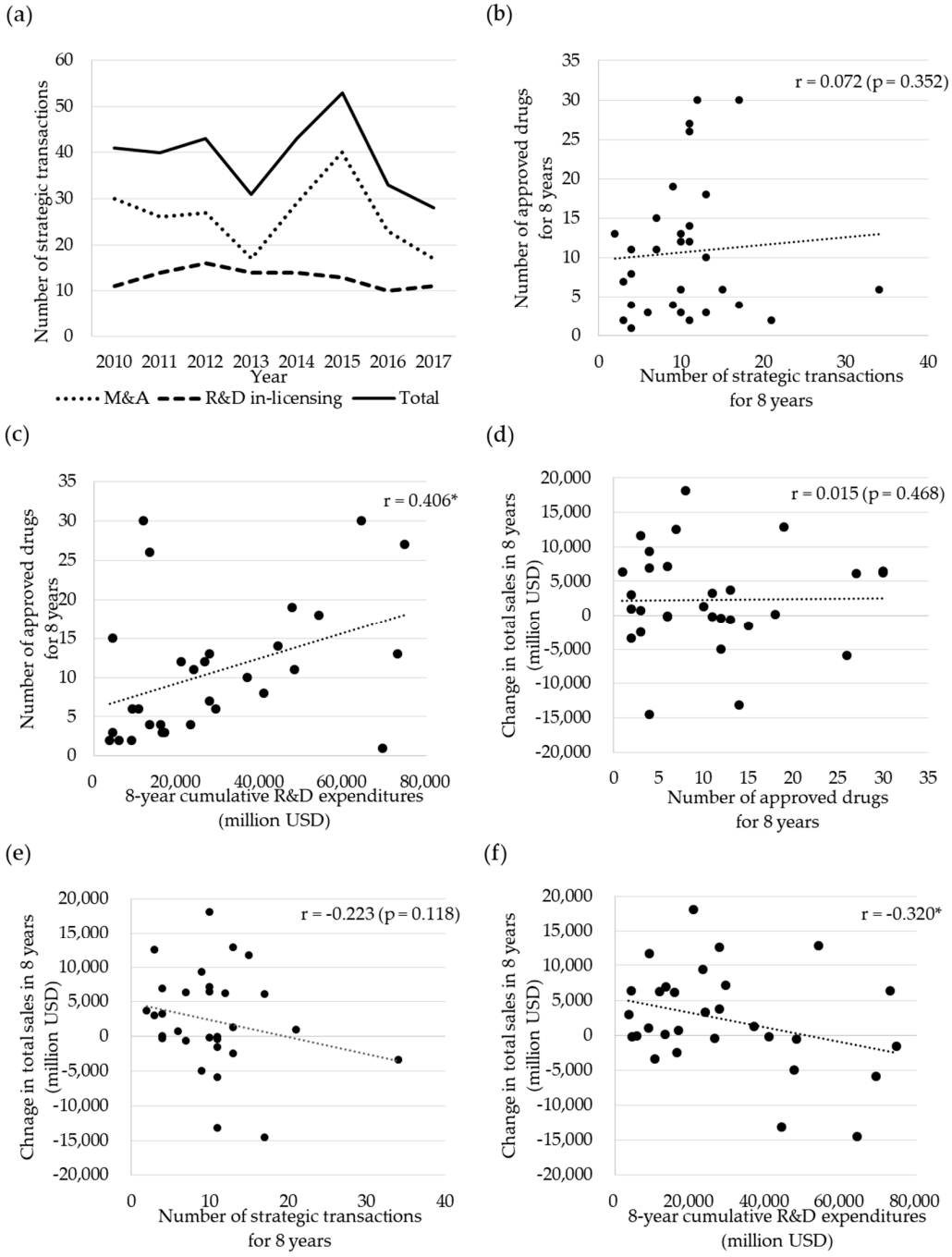

Figure 1. Trends in strategic transactions and R&D productivity. (**a**) The total number of strategic transactions each year is displayed as a solid line. The number of M&A is displayed as a thin-dotted line. The number of R&D in-licensing transactions is displayed as a thick-dotted line. (**b**) The correlation between the total number of strategic transactions from 2010 to 2017 and the total number of FDA-approved drugs (which include the new molecular entity drugs and the new biologic drugs from 2010 to 2017) is shown as a dotted line. Each black point represents a unique company (n = 30). The same hereinafter. (**c**) The correlation between cumulative R&D expenditures from 2010 to 2017 and the total number of FDA-approved drugs from 2010 to 2017 is displayed as a dotted line. (**d**) The correlation between the total number of FDA-approved drugs from 2010 to 2017 and the change in total sales from 2010 to 2017 is displayed as a dotted line. (**e**) The correlation between the total number of strategic transactions from 2010 to 2017 and the change in total sales from 2010 to 2017 is displayed as a dotted line. (**f**) The correlation between the cumulative R&D expenditures from 2010 to 2017 and the change in total sales from 2010 to 2017 is displayed as a dotted line. * $p < 0.05$; ** $p < 0.01$.

3.2. Comparison between Global Companies and Home-Region-Oriented Companies in Terms of R&D Productivity

To investigate the factors that would impact R&D productivity, we compared global companies to home-region-oriented companies based on the differences in their international strategies. Referring to the concept of case research, we chose to select polar types, given the limited number of cases, and to better compare cases, which could lead to a more sophisticated understanding [48].

We compared the differences in inputs, outputs, and outcomes between global companies and home-region-oriented companies (Figure 2). While there were no differences in the number of strategic transactions ($p = 0.203$, Mann–Whitney U test), the eight-year cumulative R&D expenditures ($p = 0.267$, Welch's t-test), or the number of approved drugs ($p = 0.101$, Student's t-test), we did identify a significant difference in the change in total sales ($p < 0.05$, Student's t-test). Specifically, the home-region-oriented companies had a higher change in total sales compared to that of global companies. We also evaluated the difference in the number of M&A and the number of R&D in-licensing transactions and found no difference between the groups ($p = 1.000$, Mann–Whitney U test; $p = 0.418$, Mann–Whitney U test, respectively). Our results indicate that home-region-oriented companies show better outcomes, but no clear relationship between inputs, outputs, and outcomes, as well as other possible factors impacting R&D productivity.

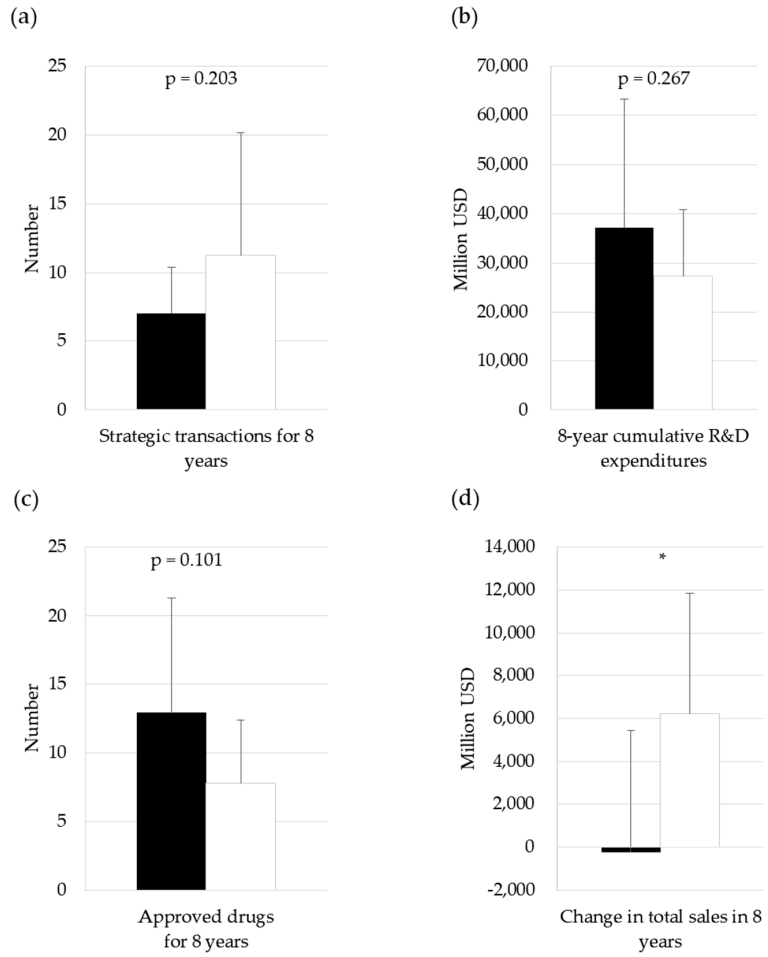

Figure 2. Comparison between global companies and home-region-oriented companies. The black bar represents global companies (n = 12), while the white bar represents home-region-oriented companies (n = 10). (**a**) The number of strategic transactions from 2010 to 2017. (**b**) The eight-year cumulative R&D expenditures from 2010 to 2017. (**c**) The number of approved drugs from 2010 to 2017. (**d**) The change in total sales from 2010 to 2017. * $p < 0.05$.

3.3. Relationship between Inputs, Outputs, and Outcomes in Terms of R&D Productivity

We performed a multiple linear regression analysis to study the relationship between inputs and outputs with the number of approved drugs as a dependent variable, and the following as independent variables: the type of international strategy, the number of strategic transactions, and the eight-year cumulative R&D expenditures (Table 2). We also analyzed the relationship between inputs, outputs, and outcomes with the change in total sales as a dependent variable and the following as independent variables: the type of international strategy, the number of strategic transactions, the eight-year cumulative R&D expenditures, and the number of approved drugs (Table 3).

Table 2. Regression analysis of the relationship between inputs, outputs, and outcomes (dependent variable: the number of approved drugs).

Independent Variable	B	β	t	*p*	VIF
Constant	2.968		1.211	0.241	
International strategy	−3.416	−0.240	−1.542	0.140	1.207
8-year cumulative R&D expenditures	0.000	0.701	4.755	0.000	1.085
Strategic transactions	0.156	0.142	0.939	0.360	1.145
R^2 (Adjusted R^2)	0.640 (0.580)				
F	10.647 ***				

*** $p < 0.001$. International strategy, a dummy variable with 0 for global and 1 for home-region-oriented.

Table 3. Regression analysis of the relationship between inputs, outputs, and outcomes (dependent variable: change in total sales).

Independent Variable	B	β	t	*p*	VIF
Constant	2828.054		0.871	0.396	
International strategy	9099.736	0.657	3.031	0.008	1.366
8-year cumulative R&D expenditures	−0.087	−0.265	−0.914	0.374	2.448
Strategic transactions	−491.310	−0.462	−2.274	0.036	1.201
Approved drugs	286.722	0.295	0.955	0.353	2.775
R^2 (Adjusted R^2)	0.640 (0.580)				
F	10.647 ***				

*** $p < 0.001$. International strategy, a dummy variable with 0 for global and 1 for home-region-oriented.

Tables 2 and 3 show the results of the regression analysis for the relationship between inputs, outputs, and outcomes. This analysis shows that the eight-year cumulative R&D expenditures have a significant positive impact on the number of approved drugs ($F = 10.647$, $R^2 = 0.580$, $p < 0.001$). This finding coincides with the trends of the pharmaceutical industry (Figure 1c). It may also be concluded that a home-region-oriented strategy has a positive impact on the change in total sales ($p < 0.01$) and the number of strategic transactions negatively impacts the change in total sales ($F = 3.017$, $R^2 = 0.278$, $p < 0.05$). Surprisingly, our results indicate that using strategic transactions to absorb external innovation did not increase R&D productivity.

3.4. Factors Impacting on R&D Productivity in the Pharmaceutical Industry

We investigated how the difference in international strategy affects the R&D strategy to determine why the international strategy affects the change in total sales. Specifically, we investigated the differences in the indications of approved drugs between the two groups. We hypothesized that global companies tended to focus more on global medical needs while home-region-oriented companies would tend to focus more on local and regional medical needs, according to a popular theory about internationalization [49]. For example, a case study of internationalization in the Indian pharmaceutical industry reported that the Indian pharmaceutical companies started developing products specifically for foreign markets to advance their global presence [50]. Thus, we compared U.S.-based global

companies with U.S.-based home-region-oriented companies to better determine how international strategy affects sales. Specifically, we evaluated differences in the proportion of drugs for cardiovascular diseases, infectious diseases, cancers, nervous system diseases, and endocrine and metabolic diseases. We focused on these indications because infectious diseases are prevalent on a global scale while cancer rates are higher in the U.S. Meanwhile, cardiovascular diseases, nerve system diseases, and endocrine and metabolic diseases are major causes of death both within the U.S. and worldwide [51,52]. We also added orphan designation as a surrogate of rare diseases because this hypothesis dictates that home-region-oriented companies tend to focus more on rare diseases entailing higher unmet medical needs in their home region.

Table 4 shows the results of these comparisons. U.S.-based global companies have a higher proportion of drugs for treating infectious diseases ($p < 0.001$, Pearson χ^2 test). Meanwhile, U.S.-based home-region-oriented companies have a higher proportion of anticancer drugs and orphan designation than U.S.-based global companies ($p < 0.01$, Pearson χ^2 test; $p < 0.01$, Pearson χ^2 test, respectively). There are no differences in the proportion of drugs for cardiovascular diseases ($p = 0.708$, Fisher's exact test), nervous system diseases ($p = 0.330$, Fisher's exact test), and endocrine and metabolic diseases ($p = 0.163$, Pearson χ^2 test). We found that U.S.-based global companies are launching products that meet global needs into the U.S. market, while home-region-oriented companies are launching products that meet local needs into the U.S. market. Thus, it was confirmed that companies implement an R&D strategy that is consistent with their international strategy. Furthermore, our results indicate that an R&D strategy focusing on a home-region orientation can increase R&D productivity.

Table 4. Comparison between global companies and home-region-oriented companies (R&D strategy).

Approved Drug Classification	Global		Home-Region-Oriented		*p*	V
	n	%	n	%		
Cardiovascular diseases					0.708	0.076
Yes	2	4.7	6	8.7		
No	41	95.3	63	91.3		
Infectious diseases					0.001	0.321 **
Yes	25	58.1	18	26.1		
No	18	41.9	51	73.9		
Cancers					0.004	0.272 **
Yes	2	4.7	18	26.1		
No	41	95.3	51	73.9		
Nervous system diseases					0.330	0.110
Yes	6	14.0	5	7.2		
No	37	86.0	64	92.8		
Endocrine and metabolic diseases					0.163	0.132
Yes	3	7.0	11	15.9		
No	40	93.0	58	84.1		
Orphan designation					0.002	0.299 **
Yes	4	9.3	25	36.2		
No	39	90.7	44	63.8		

** $p < 0.01$.

As our results indicate that the strategic transactions to absorb external innovation have not increased R&D productivity, we explored the possible cause. We performed a multiple linear regression analysis with the change in total sales as a dependent variable and the following as independent variables: the number of strategic transactions, the eight-year cumulative R&D expenditures, and the number of approved drugs. We performed this analysis for global companies and home-region-oriented companies to check if this finding applies to both groups. For home-region-oriented companies, the analysis showed that the number of strategic transactions negatively affects the change in total sales ($\beta = -0.749$, $R^2 = 0.557$, $p < 0.05$). For global companies, we did not identify a clear relationship

between the change in total sales, the number of strategic transactions, the eight-year cumulative R&D expenditures, and the number of approved drugs ($F = 1.297$, $R^2 = 0.075$, $p = 0.340$).

Prior studies regarding the internationalization of R&D have led to conflicting results. Some studies show that R&D sections are located overseas to access the best talents, while others show that R&D sections are located close to the companies' home region due to the difficulty of managing foreign R&D sections [14,53–56].

We compared global companies with home-region-oriented companies in terms of the proportion of strategic transactions in the same region. We hypothesized that the geographic strategy for strategic transactions would influence the performance of external innovation absorption.

Table 5 shows the proportion of strategic transactions in the same region. The home-region-oriented companies have a higher proportion of strategic transactions in the same region than global companies ($p < 0.05$, Pearson χ^2 test). Our results indicate that home-region-oriented R&D strategic transactions would not work as expected for the absorption of external innovation.

Table 5. Comparison between global companies and home-region-oriented companies (transactions strategy).

Geographic Perspective	Global		Home-Region-Oriented		*p*	V
	n	%	n	%		
Strategic transactions in their home region					0.045	0.142 *
Yes	30	35.3	56	49.6		
No	55	64.7	57	50.4		

* $p < 0.05$.

4. Discussion and Implications

R&D productivity is continuously declining, and it is said that the conventional model of pharmaceutical business is being broken up [57]. Thus, individual pharmaceutical companies are required to understand the right growth strategies. We examined how R&D expenditures affected the number of approved drugs in 30 large pharmaceutical companies. According to our results, higher R&D expenditures yielded more approved drugs. Our results are consistent with a prior study focusing on 13 pharmaceutical companies [42]. However, our results surprisingly show that approved drugs do not always contribute to growth in terms of total sales. Rather, large R&D expenditures negatively affect growth in terms of total sales. Although increasing R&D expenditure seems to be a straightforward strategy to increase the number of approved drugs, our results suggest that this strategy is not sustainable. More recently, pharmaceutical companies have been leveraging external R&D innovation through M&A and R&D in-licensing [16]. Our results show that 30 large pharmaceutical companies have consistently made strategic transactions (e.g., M&A and R&D in-licensing); however, there is no evidence to suggest that these strategic transactions have increased the number of approved drugs. Surprisingly, we found that the number of strategic transactions negatively affected growth in terms of total sales for home-region-oriented companies.

One of the possible reasons for this finding is the problem of absorptive capacity. According to Lubatkin et al. [58], when two companies with similar knowledge bases enter an M&A, they tend to exchange knowledge. According to Lange et al. [59], a large difference in the knowledge bases reduces the power of influence on the generation of innovation output. According to Sampson et al. [60], when technological diversity is high in R&D alliances, barriers to effective knowledge transfer arise. According to Leeuw et al. [61], diversity in the alliance portfolio negatively affects radical innovative performance as defined by the percentage of turnover due to new or significantly improved products and services. According to Choi et al. [62], international R&D alliances tend to have a smaller technological distance than international manufacturing and marketing alliances. These findings explain the absorptive capacity model, in that companies cannot absorb knowledge and technologies from new domains if they do not improve their absorptive capacity [63]. The absorptive capacity perspective suggests that

home-region-oriented companies made many strategic transactions, which increased the diversity of their external knowledge and technologies, resulting in a lack of absorptive capacity.

Another possible reason is the home-country bias. There are several research studies in which the choice of location is important [64,65]. Since pharmaceutical companies have a relative advantage at home, they seek out foreign locations that have complementary strengths to their particular technology [66]. However, this is challenging for pharmaceutical companies due to their home-country bias [56]. For example, the top 10 highly internationalized pharmaceutical companies in Europe exhibited a significant preference for local partnerships within their home country [67]. The home-country bias may be explained by the low marginal cost of maintenance of the R&D networks in the home region and the fact that the geographical dispersion of R&D sections makes the controlled flow of external knowledge more difficult. Logically, pharmaceutical companies should access the best R&D resources to capture external innovation, but home-region-oriented companies tend to make strategic transactions within their home region. In short, home-region-oriented companies neither absorb external innovation nor appropriately invest their assets and resources due to these problems. This results in many strategic transactions decreasing R&D productivity and negatively affecting the change in total sales. Our results provide important insights about the innovation capability-building strategy from the perspective of R&D productivity. Hence, we propose the following recommendations: (1) pharmaceutical companies should increase their absorptive capacity, so that they may better manage diverse external knowledge and technologies [63], and (2) pharmaceutical companies should execute "sensing", as defined by the capabilities-based entrepreneurial theory, to identify and access the right innovative capabilities, such as technologies and knowledge [68,69].

Moreover, we found that pharmaceutical companies research and develop products in line with their international strategy and home-region-oriented companies focus on research and develop new drugs that satisfy local unmet medical needs. Therefore, home-region-oriented companies have launched more orphan-drugs. Orphan drugs may achieve blockbuster status by combining several advantages of orphan drugs: faster launch with a fast regulatory review process, market exclusivity designation, premium pricing, and multiple indications for the same drug [70]. The number of rare diseases increases year by year because medical technologies are rapidly advancing at the genomic level [71]. These advances provide the opportunity to develop personalized medicine strategies as well as orphan drugs. The conventional business model relying on blockbusters focused on developing and launching a product that satisfies the medical needs in an extremely large market (e.g., H_2 blockers to treat gastric and intestinal ulcers). However, as a blockbuster strategy is not suitable for sustainable growth, the pharmaceutical industry is abandoning this strategy and moving to a niche-buster or multi-buster strategy [72]. These strategies target specific markets with niche drugs such as orphan drugs for cancer. Our results support the chain-linked model even though feedback loops would be limited in the pharmaceutical industry. Hence, we propose the following recommendations: (1) pharmaceutical companies should gather customer insights regarding unmet medical needs in the targeted market, and (2) pharmaceutical companies should research and develop cutting-edge drugs, which can create competitiveness. We believe that our recommendations will work well to increase R&D productivity. We advance a hypothesis based on our findings and prior research studies, and illustrate the relationship between inputs, outputs, and outcomes (Figure 3).

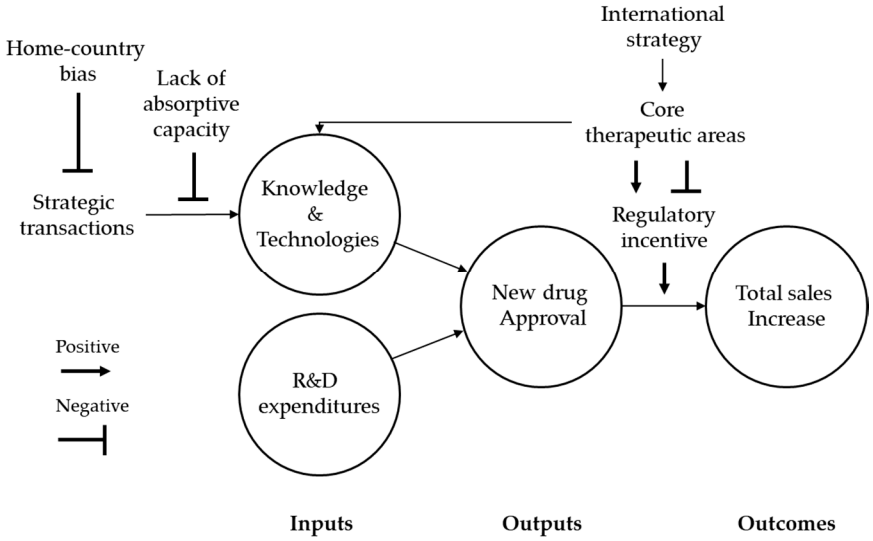

Figure 3. Assumed relationship diagram showing the factors impacting R&D productivity.

5. Conclusions, Limitation, and Future Directions

Our results suggest that it is time to change the business model for sustainable growth from the perspective of internationalization and innovation [73]. We recommend switching from the R&D model, that is dependent upon home-region-oriented external innovation and relies on blockbusters to meet global medical needs, to a model that pursues external innovation more flexibly and actively and responds to local needs by delivering more cutting-edge drugs.

Our study is an exploratory study, that is limited by its small sample size (30 large multinational pharmaceutical companies with various company sizes). Additionally, in this study, we used strategic transactions and R&D expenditures as indicators of input, approved drugs as output, and total sales as outcomes, but future research study could use technical personnel as an indicator of input, patents as output, and trademarks as outcome to investigate the effect of R&D strategy multilaterally [74]. Moreover, our study takes a quantitative approach to highlight how the R&D strategy contributes to R&D productivity. Therefore, future research studies should include a qualitative approach that utilizes interviews to gain insight into decision-making processes regarding strategic transactions. Although further research is necessary to understand how R&D strategy contributes to R&D productivity, by verifying the hypothesis drawn in Figure 3, we believe that our study contributes to the body of research on R&D productivity for sustainable growth in the pharmaceutical industry.

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