Redefinition of Value through Drug Repositioning

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Summary

Although newer drugs being developed require long-term trials and significant funding, the probability of each one's success is extremely low particularly in later years, after the creation of a new drug becomes difficult. Because Nobelpharma Co., Ltd. releases new drugs constantly (every year), it needs to pay attention to new drug development activities. Thus, the company considers its drug repositioning strategy, unlike with conventional development methods. There are four points of advantage in this strategy : (1) "large reduction of R&D cost," (2) "shortening of the R&D period," (3) "improvement of the probability of success," and (4) "the effect that the accumulation of a continuous success experience affects the organization."

When one considers drug repositioning within a framework of open innovation, it may be interpreted as a kind of licensing. Yet the contents of both things vary considerably. Under this method, a new effect from an existing drug is discovered and then sold as another (new) drug. The company utilizes the spent materials patent in another company. However, the firm does not sell the medicine in the same form and performs a redefinition of its value. The company is thus enabled to perform a redefinition of its value because knowledge has two characteristics such as accumulation and situation dependence, which is the case with a knowledge product such as a drug.

Keywords : New Drug Development, Drug Repositioning, Open Innovation, Redefinition of Value, Knowledge Product

Ⅰ Introduction

We predict that the pharmaceutical industry will experience an increase in sales as society ages, leading to increased drug consumption. However, most companies worry about future managerial uneasiness. For that reason, new drug development has an extremely big influence on a pharmaceutical company's management, making new drug development even more difficult. On the one hand, new product development is important in other product markets,

but an additional marketing mix based on 4P becomes important for new drugs. On the other hand, new product development (particularly R&D activity) is decisively important in the pharmaceutical industry. However, it remains very difficult for any company to succeed using R&D to create a new drug.

It should be emphasized that the products that the pharmaceutical industry sells are distributed between two categories : (1) “medicinal drugs” and (2) “over the counter (OTC) drugs,” for the most part. On the one hand, a medicinal drug is a pharmaceutical product prescribed for a patient in an ethical pharmacy or medical institution based on the instructions of a doctor. On the other hand, an OTC drug is a pharmaceutical product that a patient purchases from a drugstore. For these categories, 2016 product sales were, for the domestic pharmaceutical industry, 91.3% for medicinal drugs and 8.5% for OTC ones. Although some companies specialize in OTC drugs, most place an extremely high weight on the medicinal side.

Development of a medicinal drug is very difficult, and the number of new products that all pharmaceutical companies in the world combined market in a year is only around 20. In other words, most major companies cannot market a new drug for several years. The patents of the new epoch-making drugs, including Lipitor (a hyperlipidemic drug of Pfizer Corporation) expired in sequence around 2010[1]. Therefore, each company is now trying to develop the next new epoch-making drug an extremely daunting task. The development of a lifestyle-related disease drug that features an uncomplicated action mechanism is demanded in the market. Thus, advances such as hyperlipidemic drugs−an antihypertensive agent and an antiulcer agent are seen. Moreover, the furthering of new similar drugs is not very important, unlike those drugs that feature a complex action mechanism such as those for fighting cancer or Alzheimer’s. The reason that the development of innovative drugs in such fields has proven difficult is that there are innumerable proteins in the human body, and even our modern, advanced knowledge cannot elucidate all their roles and distributions. In addition, pharmaceutical molecules are too small, and thus, there is little information that can be placed upon them. Further, doing so with newer drugs is precisely the condition required (Sato, 2010).

In spite of this predicament, in recent years, the number of innovative drug development

1　In the general product market except the drug, if a starting product has a big sale, plural products that have similar function are released one after another. However, in the case of drug, the late departure company cannot sell the drug of similar efficacy and ingredient. Therefore, the development company can obtain the developer profit monopolistically during a patent period, however, when a patent expires, the sales of the development company largely decreases because some inexpensive generic drugs are marketed.

ventures specialized under R&D for such expertise has increased dramatically. Nevertheless, in new drug development, there are nagging disincentives of “the complicated process” and “the low probability of success,” and a long-term development horizon and huge funding requirements are imperative. Therefore, any innovative drug development venture lacking funding cannot continue with the necessary R&D. Under such circumstances, a type of new drug development action called drug repositioning must attract some attention. Therefore, in this study, we focus on Nobelpharma Company, Ltd., an innovative drug development venture taking a drug repositioning strategy, thus considering this strategic advantage from the viewpoint of open innovation.

This study is organized as follows. In Section 2, we summarize new drugs being developed and point out the characteristics of each one, such as “the complicated process” and “low probability of success,” then summarizing open innovation in the pharmaceutical industry. In Section 3, we focus on the new drug development activity of Nobelpharma and show its drug repositioning strategy, which is its key characteristic. In Section 4, we discuss this drug repositioning strategy from the viewpoint of open innovation. In Section 5, we summarize the findings of the study and make our recommendations for management.

Ⅱ Summary of new drug development

Ⅱ-1 R&D of the pharmaceutical company

A Key task in any new drug’s development is proving its effectiveness and safety. For pharmaceutical products, the company must prepare enormous amounts of data from various experiments that deal with concerns for side effects, since safety has a direct and significant influence on the health of a patient. Therefore, the R&D process needs a long-term horizon and massive funding. Nagasu (2012) stated that 10-15 years and perhaps 50 billion to approximately 100 billion yen must be spent to create a single new drug. Yet, there is general recognition of these requirements.

Some larger companies do repeat M&A actions in order to secure larger amounts of R&D budget and extend their scale. M&A is a characteristic of the pharmaceutical industry, and, in the total sales ranking of world pharmaceutical companies (Table 1), there are many large companies that have become gigantic through multiple M&A actions[2]. According to the R&D

2 In Japan, Astellas Pharma Inc. and Daiichi Sankyo Co., Ltd. are large companies by M&A, but domestic largest Takeda Pharmaceutical Company Limited is only the 19th place in the world because the M&A in Japan are not active as foreign countries.

Table 1　Sales and R&D Expenses of Pharmaceutical Companies (2015)

Ranking	Company Name	Sales Amount	R&D Expenses	Ranking of R&D Expenses	Sales to R&D Expenses Ratio
1	Johnson & Johnson (USA)	70,074	9,270	2	13.2
2	Roche (Switzerland)	50,065	9,963	1	19.9
3	Novartis (Switzerland)	49,414	8,935	3	18.1
4	Pfizer (USA)	48,900	7,690	4	15.7
5	Sanofi (France)	41,085	5,831	8	14.2
6	Merck (USA)	39,498	6,704	5	17.0
7	GlaxoSmithKline (UK)	36,556	5,441	9	14.9
8	Gilead Sciences (USA)	32,639	3,014	16	9.2
9	Beyer (Germany)	25,360	3,142	15	12.4
10	AstraZeneca (UK)	24,708	5,997	6	24.3
11	Abbe (USA)	22,859	4,435	11	19.4
12	Amgen (USA)	21,662	4,422	12	20.4
13	Eli Lilly (USA)	19,959	5,331	10	26.7
14	Teva (Israel)	19,652	1,525	25	7.8
15	Bristol-Myers Squibb (USA)	16,560	5,920	7	35.7
16	Boehringer Ingelheim GmbH (Germany)	16,406	3,331	14	20.3
17	Novo Nordisk A/S (Denmark)	16,041	2,023	19	12.6
18	Allergan (Ireland)	15,071	2,870	18	19.0
19	Takeda Pharmaceutical Company Limited (Japan)	15,038	2,878	17	19.1
20	Otsuka Holdings (Japan)y	11,938	1,660	23	13.9
		(Unit: 1milliondollars)	(Unit: 1milliondollars)		(%)

Source : *Monthly mix,* 2016, extra number

expenses listed in Table 1, the higher a company is ranked in terms of sales, the higher its R&D expenses. The sales to R&D expenses ratio for many companies is about 20%, indicating that the ratio of the pharmaceutical industry is much higher than the mean of the domestic manufacturing industry (4.61%).

The reason why companies spend so much on R&D is that they need vast funding for the development of epoch-making new drugs, generating huge profits if they succeed. In R&D, fierce competition arises from the fact that each firm knows that the company that creates a new drug early (and acquires a patent early) will benefit enormously. New drugs are protected by patent for 20 years and rival companies cannot sell drugs of similar efficacy and ingredients. In other words, the business model of pharmaceutical companies that create a new drug first obtain large development profits with one new epoch-making drug.

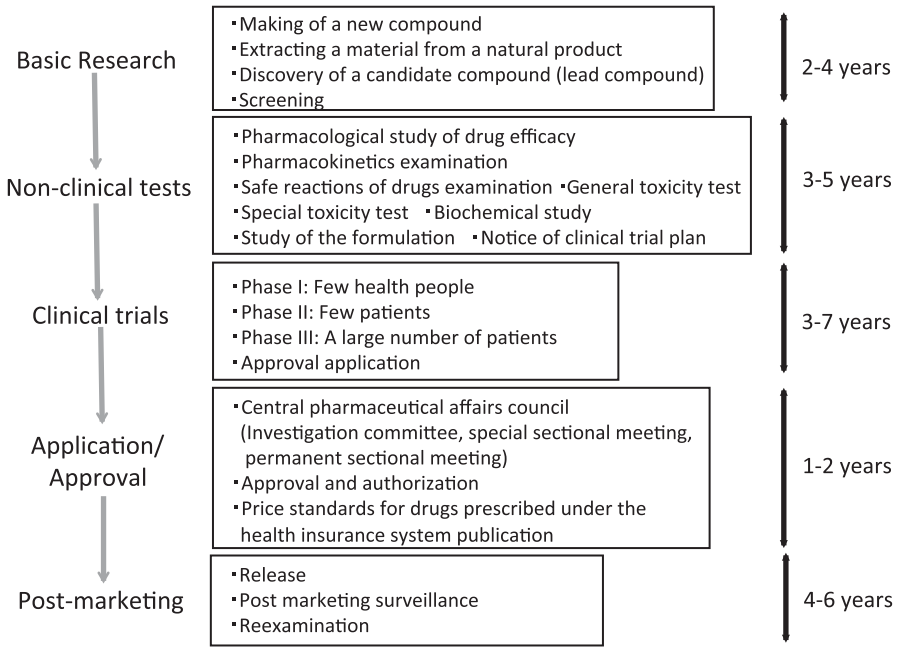
Unmet medical needs resulting from the lack of any effective therapeutic drug can expect to see increased efforts in cancer and Alzheimer's disease research. However, the development of large-scale new drugs falls faces a difficult situation, because the proteins targeted by the new drug development tend to dry up[3].

Ⅱ-2 Characteristic of R&D

Products such as cars or sophisticated electronics need anywhere from several hundred to

3　Why does a company have difficulty in creating innovative drugs though the development technology progresses every day? According to Sato (2010), this is because in a disease (high blood pressure, gastric ulcer, and bacterial infections etc.) that action mechanism is clear and plain, some drugs having high completeness were already developed. In other words, most of the diseases that are easy to make drugs are finished, and only intractable diseases such as have cancer, Alzheimer's disease, and rheumatoid arthritis been left. Furthermore, examination of the protein that could become the target of the drug already advanced, and a target considered influential has decreased.

Figure 1 R&D Process of New Drug



Source : Created from Nagao (2009) and Noguchi (2003)

tens of thousands of patents, but a drug based on only one material patent requires only two or three patents, including process patents. However, R&D processing of the new drug is extremely complicated because strict regulation impedes the approval of any new drug designed to have a big influence on human life and health. According to Pisano (2006), the biggest purpose of R&D for new drug candidates is to collect information about their effectiveness, safety, and use, and R&D is the process used to reduce uncertainty by repeating data collection and interpretation of the information. The R&D for such new drugs features two such characteristics “complicated process” and “low probability of success.”

First, in a complicated process, a company writes up the approval application for a new drug after basic research, non-clinical tests, and clinical trials, as shown in the R&D process (Figure 1). A company needs a lot of time and significant funding to test the effectiveness and safety for each process. This is especially true during data collection that occurs in the latter half of the clinical trials (from the tail end of phase II through phase III). It impels testing along with a protocol (i.e., a clinical trial plan), rarely passing through a process of trial and error. Conversely, in its fundamental research, the company does not often succeed by doing trial-and-error processes particularly.

The low probability of success is indicated in Table 2. According to this information, the accumulated probability of success before getting approval for a new drug is extremely low

Table 2 Probability of Success of New Drug Development in Japan (from 2007 to 2011)

Development Process	Compound	Probability of success	Accumulation probability of success
Synthetic compound	704,333		
Non-clinical tests starts	291	1 : 3,216	
Clinical trials starts	85	1 : 2.58	1 : 8,286
Application for approval	25	1 : 3.40	1 : 28,173
Approval acquisition	26	1 : 0.96	1 : 27,090

Note. The data of approximately 20 companies of JPMA. The total from 2007 to 2011.
Source : *DATA BOOK,* 2013

(approximately 1/30,000). Overall, the probability that a company succeeds in creating a synthetic compound during the basic research stage and can advance directly to the next stage of non-clinical tests is only 1/3,216, and the probability of success during the basic research stage is extremely low. The latter years of the R&D of a new drug are more difficult and, according to Pisano (2006), most of the R&D has to do with dealing with failure. Indeed, it may be said that most of the resources required for new drug development are spent on failures.

Ⅱ-3. Shift to open innovation

Using M&A to secure larger amounts of R&D budget are popular trends in the pharmaceutical industry. However, in recent years, strategic alliances and collaborative research have flourished, utilizing knowledge, technique, and funding. The NIH (not invented here) syndrome (Katz & Allen, 1982) was deeply rooted in the industry until several years ago. Now, companies have been increasingly advocating an open innovation strategy. Open innovation means that a company integrates an outside idea with an inside one organically, and create new value proposition (Chesbrough, 2003). Furthermore, companies have been utilizing an outside idea more than before, and facilitating other companies utilizes its idea of non-utilization more than before (Chesbrough, 2006).

Arora, Fosfuri & Gambardella (2001) point out that innovation tends to be accelerated because market buying and selling knowledge and techniques are still developing in the pharmaceutical industry. In addition, Teece (2000) suggests the possibility of separating companies that create knowledge from those that utilizing it. An innovative drug development venture develops when the company creating knowledge coexists with the one that utilizes it. Such knowledge being bought and sold highlights a shift to open innovation in the pharmaceutical industry. In this way, some pharmaceutical companies may succeed without performing the normal fundamental research, e.g., search studies, in-house buying of

knowledge (candidate material), innovative drug development ventures, only having to perform the clinical trials required in the subsequent stage. Open innovation is appropriate in the fundamental research stage, while closed innovation is basically appropriate during the clinical trials[4].

Open innovation in the pharmaceutical industry practically avoids licensing. A pharmaceutical company has a lot of opportunities to buy licenses and, under new drug development, competition with other pharmaceutical companies to buy knowledge (candidate material) from other companies that are more useful than a company's current knowledge and then perform the subsequent process of new drug development. Most sellers use innovative drug development ventures mainly to perform fundamental research. Because that stage has such a low probability of success, a key purpose of the firm is to try to raise probability of manufacturing by buying knowledge (candidate material) that went well for an earlier project. In this way, open innovation allows a firm to buy and sell useful product knowledge while still in the process of new product development. However, little licensing comes from some innovative drug development ventures (Tomita, 2015).

In summary, because the new drug process is complicated and the probability of success is low, a firm needs financial power. Nevertheless, a firm may become gigantic through M&A activity and hence manage to raise its R&D budget. Yet, that fact does not undermine the difficulty of developing new drugs with an action mechanism, e.g., curing cancer or Alzheimer's disease is complicated. Therefore, new drug development remains difficult, even though open innovation (such as licensing) is practiced.

Note the new drug development action behind Nobelpharma Co., Ltd., which markets a new drug every year while being a small venture company (see the corporate scale in the next section). Letting a firm market a new medicine with the next snarl happening every year is popular. We did this once when we were a small venture company without a corporate scale.

Ⅲ New drug development action of Nobelpharma Co., Ltd.

Nobelpharma was established in 2003 and has since increased its sales to 7,435 million yen (2015, Table 3). Nobelpharma released its first new drug in 2008 (Table 4), and its sales increased steadily the following year.

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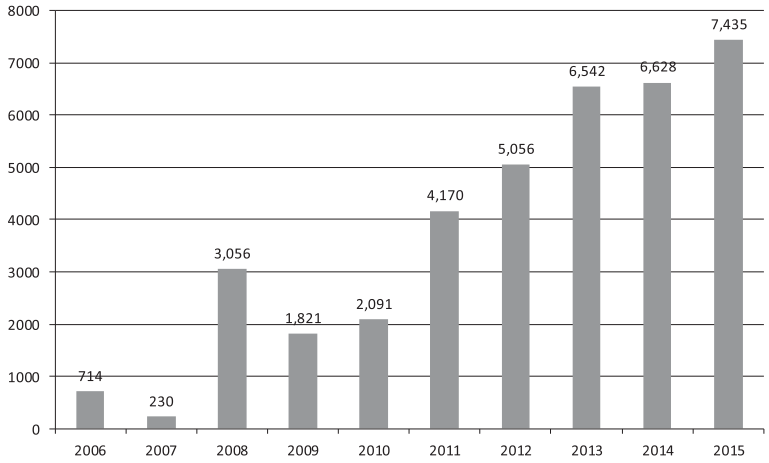
4 According to Odagiri (2007), both open science and closed science become important in a field pursuing understanding the root and practical use at the same time in the pharmaceuticals and bio technology.

Table 3　Sales of Nobelpharma



Note：unit is million yen.
Source：Created from Business Reports of Nobelpharma

Table 4　Product List of Nobelpharma

	Brand Name	Launch	Indicaitons	Licensor
1	Nobelzin capsuls Nobelzin tablets	Apr 2008 Feb 2015	Wilson's disease	Teva
2	Lunabell LD Lunabell ULD	Jul 2008 Sep 2013	Dysmenorrhea	Jansen
3	Nobelbar	Dec 2008	Neonatal seizures, Status epilepticus	In-house
4	Fostoin	Jan 2012	Status epilepticus, Prevention of postoperative seizures, etc.	Pfizer
5	Gliadel	Jan 2013	Malignant glioma	Eisai
6	Alabel	Sep 2013	Diagnosis of malignant glioma	SBI Pharmaceuticals
7	Indacin	Jan 2013	Patent ductus arteriosus of prematurity	Lundbeck
8	Cosmegen	Jan 2013	Wilms' tumor, Choriocarcinoma, Pediatric solid malignant tumor, etc.	Lundbeck
9	Unitalc	Dec2013	Prevention of recurrent malignant pleural effusion	Novatech
10	Respia	Dec 2014	Apnea of prematurity	Nippon Boehringer
11	Rapalimus	Dec 2014	Lymphangioleiomyomatosis	Pfizer
12	Zanosar	Feb 2015	Gastroenteropancreatic neuroendocrine tumor	Keocyt

Note：At February, 2015
Source：Business Report of Nobelpharma, 2015

Nobelpharma released “Novelgin capsule” to combat Wilson’s disease, making it the first therapeutic drug of April 2008[5]; they then released “Lunabell LD” to treat dysmenorrhea in July, and finally released “Nobelbar” for neonatal seizures and status epilepticus of newborns in December (Table 4). It is extremely unusual for any firm to release three drugs in a single year, even for major companies. Nevertheless, it is possible. Nobelpharma released six new

5　The onset rate of the Wilson’s disease is one of 30,000-40,000 people, and there is only the patient approximately 1,500 in Japan.

drugs in 2013[6]: “Gliadel,” “Indasin,” “Cosmegen,” “Alabel,” “Unitalc,” and “Lunabell ULD.” It released “Fostoin” last year and “Respia” and “Rapalimus” in 2014. The constant release of new drugs in the pharmaceutical industry has been unique.

Of the 12 products listed in Table 4, the sales leader has been a dysmenorrhea therapeutic drug called “Lunabell,” reaching 4,800 million yen in 2015. Originally, Lunabell was “Ortho,” developed as an oral contraceptive (pill) by Ortho McNeil Corporation of the Johnson & Johnson K.K. group (United States). In Japan, Janssen Farmer Corporation (Janssen Kyowa Co., Ltd.) approved and acquired this product as a low-dose oral contraceptive in 1999, continuing to sell it through January 2017. The experts (e.g., doctors) predicted that Lunabell was effective against dysmenorrhea and endometriosis as a hormone preparation since both estrogen and progesterone are included as ingredients of the female sex hormone mixture. Nobelpharma captured the tacit knowledge and, using this drug’s effect as a hypothesis, bought Ortho from Janssen Farmer Corporation. Nobelpharma decided that the indications for dysmenorrhea coupled with endometriosis were treatable with the drug and collected the necessary clinical trial data that later confirmed its effectiveness, leading to it being manufactured as “Lunabell” in 2008.

In Table 4, one can see that the only in-house developed products are “Nobelbar” and “Lunabell ULD.” Different companies introduced the other drugs. Similar to Lunabell, Nobelpharma chose the drug that had already been sold under its original adaptation, and from it, developed a new drug that targeted a new adaptation. The ability to do so has been an excellent strategic characteristic of Nobelpharma. Considering the fact that the drug had already been sold, its re-approval was readily accomplished and, in other words, its safety had already been proven. As for the drug itself, any single side effect raises concerns over its influence on the human body directly. Therefore, a company must prepare an enormous amount of data to prove its safety during clinical trials. This presents a big problem in the pharmaceutical industry, requiring many years and huge funding. Re-utilizing such drugs avoids this hassle, since the company must only prove its effectiveness for the new adaptation. This effect is clearly shown in the figures of Table 5.

On the one hand, the average time required for clinical trials is 3-7 years (Figure 1), but in recent years, companies have wasted approximately 5-7 years, practically speaking. On the other hand, according to Table 5, Nobelpharma has succeed in reducing clinical trial times considerably, cutting the 29.45-month average to just two to one-half years.

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6 Lunabell ULD is approved as a new feature unlike the existing drug Lunabell LD and new dose pharmaceutical products.

Table 5 Clinical Trials Times of Nobelpharma

Brand Name	Development Period
Nobelzin capsuls	21
Lunabell LD	39
Nobelbar	24
Fostoin	24
Gliadel	32
Alabel	27
Ulunabell ULD	40
Unitalc	42
Respia	28
Rapalimus	16
Zanosar	31
Avarage	29.45

(Unit: month)

Source : Created from document of Nobelpharma

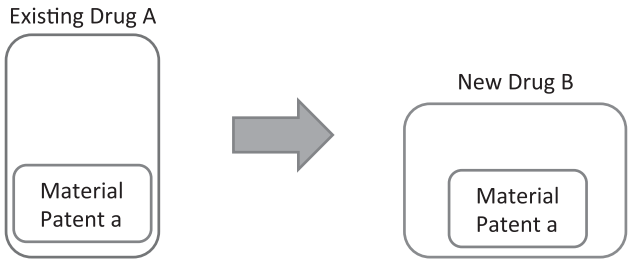
The pharmaceutical products that Nobelpharma develops are orphan drugs. Such drugs are designed against diseases that affect relatively few patients (under 50,000 target patients in Japan), and there are no substitute pharmaceutical products or ancillary therapeutic methods in use. Pharmaceutical products are in high demand and can cure unmet medical needs. Therefore, in the United States, the development company is granted extraordinary merit through the Orphan Drug Act (1983), and, thus, receives favorable tax treatment and the grant in Japan. The reason for such legislation is that the amount of money required for R&D is the same, regardless of the number of patients. In other words, it is difficult to secure profits with orphan drugs that correspond to the investment, unless a company can somehow have bigger sales and profits through fewer patients. Therefore, orphan drugs are a niche market with a few rivals, since other firms tend not to enter into their development.

Ⅳ Discussion

Ⅳ-1 Advantage of drug repositioning strategy

Because the orphan drug provides little profit for any new drug, a developing company wants to reduce its R&D cost as much as possible. Accordingly, Nobelpharma has found different adaptations from drugs previously sold by other companies and thus brings about new efficacy. This activity is called drug repositioning. In doing so, a company changes a drug's perspective by developing an ingredient of an existing drug A that becomes a material patent as a different adaptive new drug B (Figure 2). Most of the products of Nobelpharma, including "Lunabell" of the dysmenorrhea family that was originally billed as an oral contraceptive (pill), correspond to such drug repositioning.

Figure 2 Summary of Drug Repositioning



Because a company wants to develop new orphan drugs at lower cost, the development period must be shortened as much as possible, avoiding the use of more resources. In addition, the new drug's development faces a predominantly high probability of failure. Indeed, a great deal of money that was invested becomes buried when it cannot be manufactured during the middle stage R&D. Therefore, the company seeks assurances prior to its manufacture. Because safety concerns have already been eliminated for existing drugs previously sold by other companies, a firm must only prove the new adaptive aspect's effectiveness. In other words, the company can omit some fundamental research, such as basic research and non-clinical tests, and can start right away with the clinical trials. The company can thus compress costs considerably by saving time and money spent on fundamental research. Because innovative drug development ventures often require such resource expenditure, and often cannot finish clinical trials due to financial difficulties, thus cancelling its R&D, one can clearly grasp the significance of omitting fundamental research entails.

Performing R&D from clinical trials without fundamental research specializes in D (development ; or the clinical trials) of the R&D process, and cutting off R (research ; or fundamental research such as basic research and any non-clinical tests), and thus Nobelpharma does not have to establish a research institute. The fictitious scene of a researcher in a white robe waving a flask containing a drug and conducting experiments is part of fundamental research, whereas clinical trials are performed in cooperating medical institutions. Hence, the company does not necessarily need a research institute and can cut costs significantly.

We were able to realize "large reductions in R&D cost" and accomplish a "shortening of the R&D period" mentioned above, which are advantages of using the drug repositioning strategy, and we can point out "improvement to the probability of success" and "the effect of how the accumulation of continuous successful experiences affects the organization." According to Table 2, the probability of success during the basic research stage (1/3,216) is predominantly lower than during non-clinical tests (1/2.58) or during clinical trials (1/3.40). Thus, the probability of success rises markedly if a company can pass the basic research stage.

Table 6 Possibility of Drug Repositioning Strategy

	Blockbuster	Orphan Drug
Conventional New Drug Development	○	△
Drug Repositioning	△	○

A researcher engaged in basic research may not find candidate material tied to a new drug's development for a decade or two. However, when he can participate in the manufacture of new drugs constantly, his morale will increase. When work satisfaction, passion, and the spirit of self-advancement are increased by the accumulation of continuous experiences of success, a significant, positive effect is felt throughout the organization[7].

Should developers of blockbuster (epoch-making) new drugs also practice the drug repositioning strategy? Alternatively, is it effective only for the development of orphan drugs? We summarize this in Table 6. Conventional new drug development requires lots of time and money. Therefore, this method is hardly suitable for those who want to get rich quickly rather than a patient company that develops a blockbuster. Thus, on the one hand, the left upper cell of Table 6 is denoted as "○." On the other hand, a company cannot collect the profits it requires if it spends large amounts of resources on orphan drugs. Therefore, while it is a proper development method, few companies actually enter such production. The cell of the top right corner, therefore, becomes "△." Thus, we want to pay attention to drug repositioning. This aspect is suitable for the development of orphan drugs, as we argued in this section. Thus, the lower right cell becomes "○." The problem is the case in the lower left cell.

As drug repositioning strategy was enabled, we could point out two phenomena. One is that a company was able to collate big data for drugs with a gene more easily. The other is that a company immediately understood the relations between a disease and the gene. For example, aspirin was the alleviation of fever and painkiller, which Bayer AG developed in 1897, but another company is developing another one that assumes its adaption for colon cancer and large intestine polyps. In drug repositioning, a characteristic use of the existing drug that has already been proven safe is desirable in the development blockbusters as well. However, it is difficult to apply existing drugs in that case since there are action mechanisms that are complicated, e.g., for targets like cancer or Alzheimer's disease. With these parameters, the lower left cell becomes "△."

7 Because the reduction of R&D cost can lower the drug price, it is also a merit for the patients.

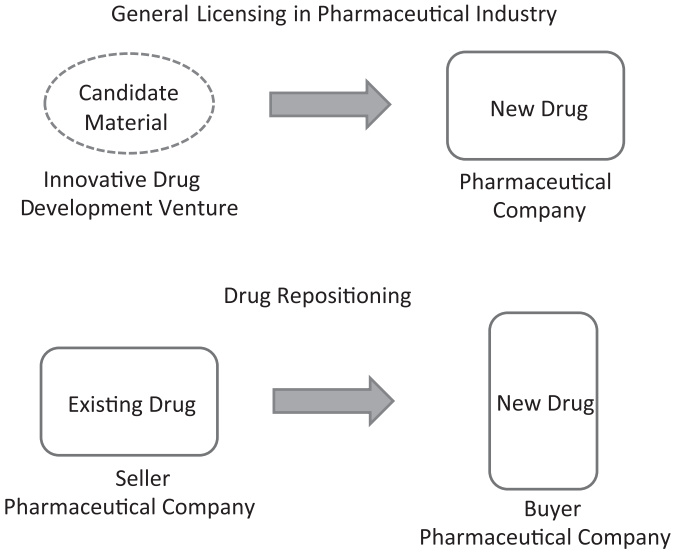
Ⅳ-2. From the viewpoint of open innovation

When we understand drug repositioning from an open innovation perspective, we can say it is a form of licensing. However, the contents are different from the licensing that is often practiced in the pharmaceutical industry, with differences seen in Figure 3.

At first, licensing was often practiced in the pharmaceutical industry. A company purchased the candidate material that seemed to become a new drug from an innovative drug development venture and carries on the subsequent development process. By buying and selling patent rights, its usefulness will likely move. As the opportunity for business is carried out, the sales promotion garnered from an innovative drug development venture begins. The innovative drug development venture wants to sell the candidate material and make a profit through licensing the middle stage of the R&D process, mainly because it did not have the funding depth to tolerate the whole development process in the first place. The purpose of this business for a buyer increases the speedup aspect and the probability of success with the new drug's development.

Under drug repositioning strategy, a company finds out the drug that seems to work for a different disease by looking at the existing drug of another company, thus developing a new adaptation for it. The process is accompanied by buying and selling patent rights, but the seller does not lose its possibility of marketing the existing drug. Because the seller does not lose its distribution for the existing drug, it does not suffer any loss and can profit by licensing the drug. The buyer takes the existing drug that seems able to be used in a new drug, and business begins. The buyer then attempts to shorten the R&D period and reduce R&

Figure 3 Licensing and Drug Repositioning



D funding, as safety issues have already been cleared. This model differs greatly from the conventional business one, trying to create a blockbuster via large R&D expenditures.

In drug repositioning, a material patent must be bought and sold, and some action to newly capture a material patent must be performed. It is the starting point of the R&D that a company creates an idea (hypothesis) such as "because compound △△ coordinates function ○○ of a protein YY, it is able to treat disease XX safely" in the R&D of the new drug ; however, a company creates an idea (hypothesis) about another disease □□ in drug repositioning. In brief, the company redefines the value of an existing product.

This redefinition of value is not easy. However, a company easily redefines an existing drug because its material patent is a lump of knowledge product, featuring accumulation characteristics. In other words, knowledge is piled onto existing knowledge. Thus, the knowledge created at a certain point is the latest knowledge and a finished product, but a company can create even more new knowledge than was previously developed from that point on. In other words, a knowledge product is always developing and never in a completed form. In addition, it is seldom the case that all of the knowledge required for a new product's development is created from scratch ; the company must piece the existing knowledge together. In the case of knowledge products, action to define the value of an existing product again is important.

As another characteristic of the knowledge, we can point out situational dependence. The knowledge varies in value according to the person who see it, the person who use it, and that value differs, too, according to the situation that each person is subjected to. There is valuable knowledge for all people and companies from such products, too. However, when accumulated knowledge is high, its value becomes meaningful only to certain people and companies in specific situations. For example, for specific knowledge, the researcher engaging in new product development called AA finds special value in something, but another researcher developing BB may not. They evaluate the value of a knowledge product suitable for their research agendas and redefine its value accordingly.

In brief, redefining an existing product's value is effective because of its cost-cutting merits, but not easy. However, companies can do it because of two characteristics : accumulation and situational dependence.

Finally, the reason that Nobelpharma has been successful in the practice is because the new drug development process does not end after its release. The company must attract information about whether there are serious side effects. Therefore, after a new product release, an MR (a medical representative) who does business of the pharmaceutical company visits medical

institutions (customers) and gathers side-effect information from doctors continuously. It is the main purpose for his visit. Businesspeople from Nobelpharma also visit them to collect tacit knowledge from doctors citing reasons like “because Ortho includes estrogen and progesterone, which are ingredients of the female sex hormone, I think that it has an effect for dysmenorrhea and an endometriosis as hormone preparation.” Because they always set up such antennae, they can obtain hints about new drug development[8].

Ⅴ Conclusion

We considered that “large reductions in R&D cost,” “shortening of the R&D period,” “improvement of the probability of success,” and “the accumulation of continuous successful experiences positively affects the organization” are advantages of drug repositioning strategy, highlighting the case of Nobelpharma.

When we think about drug repositioning in a framework of open innovation, we can interpret it as a kind of licensing, but the contents of both vary widely. On the one hand, in open innovation, a company buys candidate material to develop further and thus succeeds in a subsequent development process. On the other hand, in drug repositioning, a company discovers a new effect and buys a material patent from an existing drug offered by another company. Chesbrough (2003) points out the need to sell intellectual property that is not used in companies for open innovation. However, drug repositioning strategy entails purchasing an occupied material patent from another company. The company does not sell it in the same form and redefine value because the product is suitable for redefinition if the value exists. For example, drug repositioning becomes more effective with orphan drugs than blockbusters. Thus, a company must decide what kind of product is most suitable.

Finally, there are two suggestions for management. First, utilize existing knowledge again. Schumpeter (1934) asserted that innovation is the recombination of existing knowledge, and a company can utilize existing knowledge as a new product by interpreting existing knowledge from new viewpoints. In this case, a company may pay more attention to existing knowledge in the company’s efforts conventionally. However, in these days of shifting to open

8 Generally, a pharmaceutical company and an innovative drug development venture have expertise every company and perform new drug development based on the existing knowledge, technique, and results of research accumulated to a research institute and the individual researcher. Thus, many companies that are not active in collecting information about the material of the new drug candidate out of the company exist. Therefore, consciousness for MSL (medical science liaison) which performs mainly collecting information from a doctor increases between world major companies.

innovation, a company must sometimes pay more attention to used knowledge now from other companies and competitors. “Exploitation” and “exploration” of knowledge (March, 1991 ; Levinthal & March, 1993) in new product development becomes increasingly important.

Second, reinforce managerial perspectives pertaining to R&D. Because many companies often fail in the R&D stage without being able to manufacture a product, they need a great deal of available funding. On the other hand, it is difficult to control R&D costs, and the cost-awareness of a research institute and its researchers is low. However, if a company can utilize existing knowledge again, it can greatly reduce development costs. Therefore, a company should raise awareness regarding costs. Currently, Nobelpharma does not own a research institute because it recycles existing knowledge. In addition, the morale of the organization has increased by succeeding in R&D continuously.

References

Arora, A., A. Fosfuri and A. Gambardella (2001), *Markets for Technology : The Economics of Innovation and Corporate Strategy,* Cambridge, MA : MIT Press.

Chesbrough, H. (2003), *Open Innovation : The New Imperative for Creating and Profiting from Technology,* Boston, MA : Harvard Business School Press.

Chesbrough, H. (2006), *Open Business Models : How to Thrive in the New Innovation Landscape,* Boston, MA : Harvard Business School Press.

Katz, R. and T. J. Allen (1982), “Investigating the Not Invented Here (NIH) Syndrome : A Look at the Performance, Tenure, and Communication Patterns of 50 R&D Project Groups,” *R&D Management,* Vol.12, No.1, pp.7-19.

Levinthal, D. A. and J. G. March (1993), “The Myopia of Learning,” *Strategic Management Journal,* Vol.14, Winter Special Issue, pp.95-112.

March, J. G. (1991), “Explanation and Exploitation in Organizational Learning,” *Organization Science,* Vol.2, No 1, pp.71-87.

Pisano, G. P. (2006), *Science Business,* Boston, MA : Harvard Business School Press.

Schumpeter, J. A. (1934), *The Theory of Economic Development : An Inquiry into Profits, Capital, Credit, Interest, and the Business Cycle,* Cambridge, MA : Harvard University Press.

Teece, D. J. (2000), *Managing Intellectual Capital : Organizational, Strategic, and Policy Dimensions,* Oxford : Oxford University Press.

(in Japanese)

Nagao, T. (2009), *Yoku Wakaru Iyakuhin Goukai* [*Pharmaceutical Industry to Know Well*] Tokyo : Nippon Jitsugyou Shuppansha.

Nagasu, T. (2012), “Souyaku Kenkyuu no tameno Kagoubutsu Kanri Sisutemu [Administration System of Compound for Innovative Drug Development Studies],” *Akamon Manejimento Rebyuu* [*Akamon Management Review*], Vol.11, No.11, pp.757-765.

Noguchi, M. (2003), *Yoku Wakaru Iyakuhin Goukai* [*Pharmaceutical Industry to Know Well*] Tokyo : Nippon Jitsugyou Shuppansha.

Odagiri H. (2007), “Oupun & Kurouzudo Saiensu no Kyouzon wo Motomete [For Coexistence of Open & Closed Science],” *Hitotsubashi Bijinesu Rebyuu* [*Hitotsubashi Business Review*], vol.54, No.4, pp.62-75.

Sato, R. (2010), *Iyakuhin Kuraishisu* [*Pharmaceutical Products Crisis*], Tokyo : Shinchosha.
Tomita, K. (2015), *Chishiki Marketing* [*Knowledge Marketing*], Tokyo : Chuo Keizaisha.
"*DATA BOOK 2013*" Nippon Seiyaku Kogyo Kyoukai.
"*Monthly Mix 2016 Extra Number*" Mix.

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