# The Current Status and Value Creation of Unlisted Biotech Drug Discovery/Development Firms (Biotech DDFs) in Japan: A Holistic Approach

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*Abstract*--**Biotech Drug Discovery/Development Firms (Biotech DDFs), biotech firms that aim to discover and develop drugs, have recently started playing an important role in creating new drugs alongside traditional pharmaceutical companies. With the intention of proposing a policy that resolves issues concerning the cultivation of Biotech DDFs in Japan, we examined 44 unlisted Biotech DDFs through a comprehensive investigation using public domain information and commercial databases. We then analyzed the patents, and research and development pipelines, which are the key sources of Biotech DDF's enterprise value.**

**The results of profiling and subsequent analysis indicated that most of the clinical compounds by Japanese unlisted Biotech DDFs are currently in a development stage where there is little possibility that they will be approved as pharmaceutical products. The results also showed that the patents of Japanese unlisted Biotech DDFs are heavily dependent on academia.**

**We revealed that the industrial base for Japanese unlisted Biotech DDFs is still weak even though the government's innovation policies have made large financial supports for academia research to build up the biotech industry for one of leading sectors. This result according to our holistic approach suggests that effective measures to strengthen Japanese Biotech DDFs need be proposed.**

## I. INTRODUCTION

In June 2013, the Abe administration launched the "Japan Revitalization Strategy – Japan Is Back," which set out three action plans to achieve the Roadmap to Growth: the Plan for the Revitalization of Japanese Industry; the Strategic Market Creation Plan; and the Strategy of Global Outreach.[1)] The importance of the pharmaceutical and medical device industry in providing products and services of higher added value in Japan, which lacks natural resources, has been particularly noted in the Strategic Market Creation Plan, which positions the health and longevity of industry as one of its strategic focus areas.

The Japanese pharmaceutical industry has an impressive record. Since the 1990s, it has produced a large number of globally selling drugs, including a number of blockbuster drugs (drugs that generate more than 100 billion JPY of turnover each year). All these drugs are low-molecular-weight compounds, and they were created using technologies in which Japan is particularly knowledgeable, such as organic synthesis and fermentation technology. However, in recent years, the productivity of new drug development has declined considerably. This is attributable to a number of factors, including a decline in potential drug targets, the increasing difficulty in acquiring clinical data superior to existing drugs, and a steep rise in the development costs of conducting long-term clinical studies on a large number of patients [14].

On the other hand, biologics such as antibodies, which target the cause of disease or the elements that contribute to the development of disease, have been shown to have universal utility as pharmaceutical products. They have made a marked contribution to the development of new drugs by biotech firms, which possess cutting-edge scientific technologies that differ from the drug-creation technologies used by traditional pharmaceutical companies. According to a report in 2010 by Kneller, biotech firms drove forward the development of about half of all U.S.-originated new drugs approved in the U.S. [6].

Accordingly, to further develop the Japanese pharmaceutical industry, it will be essential to forge alliances with Biotech Drug Discovery/Development Firms (Biotech DDFs) in Japan, which are close geographically and have a high degree of culture-based mutual understanding. To this end, we launched policy research and advocacy focusing on the cultivation of Biotech DDFs. Specifically, we conducted a fact-finding investigation of Biotech DDFs in Japan to identify the problems they face.

The Japan Bioindustry Association (JBA) has been conducting an ongoing fact-finding study of Japanese biotech firms since 2002. In its recently published "2013 Survey of Bio-venture Statistics and Trends," JBA reported that, as of January, 2013, there were 552 biotech firms (617, if firms over 20-years old are included) with a business size (mean/median) of 234.4/64.0 million JPY turnover, -42.4/1.3 million JPY operating profit/loss, 304.6/35.0 million JPY capital, and 15.6/7.0 employees.[2)] The survey sampled not only Biotech DDFs, but also biotech firms that operate in a wide range of sectors including healthcare, agriculture, forestry and fisheries, environmental/energy, research support, production on assignment, as well as the service sector.

For a drug development firm to bring a new drug to market, it is said to take between 9 to 17 years and require over 50 billion JPY in research and development costs.[3)] Moreover, only one out of 30 thousand plus compounds succeeds in becoming a product. Such a miniscule likelihood

1) Website of the Prime Minister of Japan and his Cabinet: http://www.kantei.go.jp/foreign/96_abe/documents/2013/1200485_7321.html

2) Japan Bioindustry Association, October 2013: http://www.jba.or.jp/pc/archive/publication/admission/13_innovation_statistic_summary.pdf

3) Japan Pharmaceutical Manufacturers Association DATABOOK2012

of success means that such firms take a huge risk in advancing research and development. Therefore, Biotech DDFs hold a special position among biotech firms, and a detailed understanding of their actual business status is required to formulate policies that support them. It is simple enough to grasp the business status of listed Biotech DDFs since they regularly disclose corporate information, in addition to the fact that they have gone public by satisfying the listing guidelines set by the Market of the High-growth and Emerging Stocks (Mothers) in the Tokyo Stock Exchange (TSE).[4)] We therefore conducted an investigation of unlisted Biotech DDFs, where information disclosure is limited, as a fact-finding analysis of their value creation.

In this report, we provide the background and purpose of the research in the Introduction. We next present prior research on Japanese biotech firms in Chapter 2, and lay out the points that we aim to clarify in the study. In Chapter 3, we set out the selection criteria for unlisted Biotech DDFs, and the investigation methods such as the information collected to construct an integrated database and the sources of this information. In Chapter 4, we show the current situation of Japanese Biotech DDFs, and analyze the actual status of value creation. In Chapter 5, we discuss our fact-findings, and outline the study limitations and the outlook for future research. In the final chapter, we present the conclusion of the study.

## II. PRIOR RESEARCH AND RESEARCH OBJECTIVES

### *A. Prior Research*

Honjo and Nagaoka *et al.* have been conducting a comprehensive study of Japanese biotech firms. When JBA conducted its above-mentioned yearly trends survey, they added survey items concerning the growth process of Japanese biotech firms since their market entry [2], the procurement of funding for research and development, change in core technology, alliance situation and patent system [3], company representatives [4], and scientific sources [5].

In addition, Motohashi released a report on the quantitative comparison of Japanese and U.S. firms based on firm level data (Japan: 443 firms [of which 12 were listed], U.S.: 1,446 firms [of which 431 were listed]) [9]. According to this report, Japanese biotech firms are of a much smaller scale than U.S. biotech firms. However, unlike their U.S. counterparts, the size of these Japanese firms grows over time, which suggests that the business model followed by a Japanese firm is different from that followed by a U.S. firm. These results also suggest that, rather than investing vast sums in high-risk research projects, Japanese biotech firms are earning their "daily bread" by providing research services in low-risk sectors. It is suggested that a major factor behind the discrepancies between Japanese and U.S. biotech firms is the difference in their funding environment, specifically concerning Venture Capital firms (VCs).

Eyo reported the results of a comparison of Japanese biotech firms with biotech firms in the U.S., the U.K., and Germany [1]. Eyo pointed out that, despite the presence of a large market and established biotechnologies such as fermentation and bioprocess engineering, Japan considerably lags behind the bioindustry in the West in terms of turnover/profit and size of workforce. As with Motohashi, Eyo has identified Japan's approach to VC funding as a problem.

### *B. Research Objectives*

All of these prior studies described above have targeted the entire population of Japanese biotech firms. We have focused our research on Biotech DDFs, which, compared to other biotech firms, are involved in drug development that entails a high level of uncertainty, a long time frame and vast funds. In this paper, we have built a comprehensive corporate database to achieve the following:

1) Present the business strategies and business status of Japan's unlisted Biotech DDFs: This includes turnover/profit, capital, career background of President/CEO, size of workforce, research and development pipeline (a series of projects that have progressed beyond the stage of pre-clinical studies), alliances, and patents.
2) Analyze the relationship between business results and firms' characteristic profiles, and discuss the potential of Japanese Biotech DDFs for contributing to the creation of new drugs.

## III. METHODOLOGY

Of the 660 firms listed at the end of the "2012 Survey of Bio-venture Statistics and Trends" from JBA, we selected 195 firms classified under the "Pharmaceutical Products" or "Other" subcategories, which were grouped under "Medical and Healthcare." We visited the company websites to confirm the information regarding business description and research and development pipeline, and then deemed 48 firms as unlisted Biotech DDFs. We made use of public domain information as well as commercial database information to gather data shown in Figure 1 [15, 10, 13, 11]. In addition, to examine the business strategy and the career background of the President/CEO, we finally sampled 44 firms that presented relevant data on their company websites as of December 2013.[5)]

4) The chapter in the TSE New Listing Guidebook 2013 "Mothers VI: Q&A concerning Criteria for Listing, 2: Other (1) Bio Businesses for Drug Discovery/Development" (p.109 (2013)), outlines seven requirements for listing (e.g. "Does the pipeline contain compounds that are confirmed, to a reasonable degree, in clinical studies to show medical efficacy?" "For the primary pipeline, are measures employed to secure long-term development and commercialization (manufacture, marketing, etc.) by way of alliances with pharmaceutical companies, etc.?")

5) Included in the 44 unlisted Biotech DDFs sampled in this survey is Oncolys BioPharma, which was listed on the TSE Mothers Market on

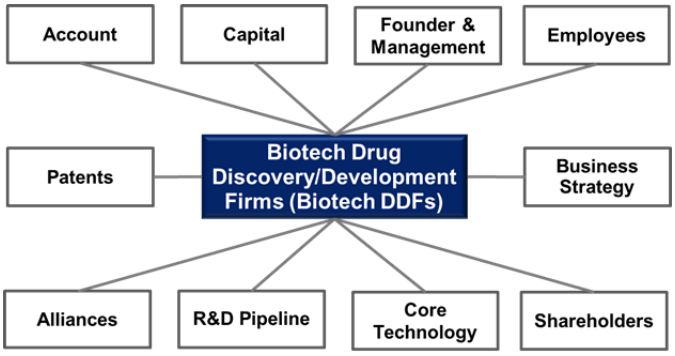


Figure 1. Information to be Collected

We have defined a Biotech DDF as a firm that fits the JBA definition of a biotech firm[6], and whose business activities, in whole or in part, fit one or both of the following descriptions: a "firm that has a drug candidate under clinical development (irrespective of origin) and conducts development activities with the aim of getting the drug candidate approved as a pharmaceutical product as stipulated by the Pharmaceutical Affairs Law," or a "firm that does not have a drug candidate under clinical development, but conducts drug discovery and pre-clinical research with a view to carry out clinical development or license a drug candidate to a third party." Therefore, biotech firms whose business is in fields that are not regulated by the Pharmaceutical Affairs Law, such as cellular therapy or regenerative medicine, were not included among the Biotech DDFs sampled in this study.

We referred to company websites for information on company overview, history of company development, management information, and business strategy. In terms of accounts/financial information, capital information, research and development pipeline/ partner information, and patent information, we used the commercially available databases: BUREAU VAN DIJK "Orbis," Japan Venture Research "Premium Service," Thomson Reuters "Integrity," and Thomson Reuters "Derwent Innovations Index." Specifically, for accounts/financial information, we used "Orbis" as of December 2013; for capital information, we used "Premium Service" as of August 2013; for the research and development pipeline/ partner information, we used "Integrity" as of August 2013 and company websites as of December 2013; and for patent information, we used the "Derwent Innovations Index" as of August-November 2013.

December 6, 2013. Moreover, Mebiopharm, which was delisted from the TSE TOKYO PRO Market on June 7, 2013, is not included.

6) The JBA definition is that a biotech firm is a firm that meets all four of the following criteria:
(1) The company utilizes, or develops for, biotechnology; (2) The number of employees complies with the definition stipulated by Japan's "Small and Medium Enterprise Basic Law;" (3) The company is less than 20 years old; (4) The company's primary operations involve research and development, contract research service, manufacturing, or advanced scientific consulting.

## IV. RESULTS AND ANALYSES

### *A. Basic Information on Unlisted Biotech DDFs*

We have shown the overall investigation results for all 44 unlisted Biotech DDFs sampled regarding year of foundation, origin of business, business strategy, turnover, net profit/loss, stated capital, career background of President/CEO, size of workforce, research and development pipeline, and patents. As mentioned in Chapter III, Methodology, this data is based on public domain and commercial database information; meaning, that we did not acquire all of the data for the 44 firms.

#### 1) Year of Foundation

Eight of the 44 unlisted Biotech DDFs, the largest percentage, were founded in 2004; seven of the firms were founded in 2003; six firms were founded in 2001; and the average age was 9.7 years. Comparing this to 10.9 years, the average age of the 15 companies that were confirmed as listed Biotech DDFs in the JBA list used in this study, the unlisted firms appear to be younger. It is worth noting that only two firms were founded after the global financial crisis of 2008. While it is possible that the JBA survey may not have accurately captured the data concerning newly founded Biotech DDFs, it is highly likely that the insufficient supply of VC and other forms of risk money had a significant impact on the Biotech DDFs engaged in drug development business that entails vast research and development costs.

#### 2) Origin of Business

Referring to the information from the company websites, we grouped the investigated firms into four categories based on the technical sources that formed the origin of business. These are "Academia Source Firms" (firms that were founded based on academic research outcomes, for example, those that explicitly state on their profile that they are university-originated), "JV Business Source Firms" (firms that were formed following industrial-government joint venture (JV) business conducted for a fixed period), "License Source Firms" (firms that started businesses based on the licenses of marketed products and clinical compounds which have not yet undergone clinical studies in Japan), and "Individual or Unidentified Source Firms" (firms that are considered to be based on the founder's individual research outcomes, or firms that have not clearly indicated sources). Twenty-five firms were considered "Academia Source Firms" (57%), two firms were considered "JV Business Source Firms" (5%), eight firms were considered "License Source Firms" (18%), and nine firms were considered "Individual or Unidentified Source Firms" (20%) (see Table 1).

#### 3) Business Strategy

For business strategy, we examined the firms' technical strength, therapeutic area of focus, and presence/absence of business projects outside of drug development (e.g., research support business). Since some firms fit multiple criteria and

TABLE 1. RELATIONSHIP BETWEEN FIRM GROUPS BY ORIGIN OF BUSINESS AND PATENTS GRANTED

| Firm Group by Origin of Business | Firms | | Domestic Patents Granted | | Foreign Patents Granted | |
|---|---|---|---|---|---|---|
| | Number | Ratio (%) | Mean Number | Mean Granted Rate (%) | Mean Number | Mean Granted Rate (%) |
| Academia Source Firms | 25 | 56.8% | **5.7** | **31.0%** | **3.6**$^{¶}$ | **29.8%** |
| JV Business Source Firms | 2 | 4.5% | **15.0**$^{*}$ | 24.4% | **18.0**$^{¶,†,‡}$ | **48.6%** |
| License Source Firms | 8 | 18.2% | 3.5 | **40.2%** | 2.6$^{†}$ | 23.0% |
| Individual or Unidentified Source Firms | 9 | 20.5% | 2.8$^{*}$ | 21.5% | 0.8$^{‡}$ | 17.6% |
| All Firms | 44 | 100.0% | 5.1 | 30.4% | 3.5 | 26.9% |

Note: Significant differences were shown at $p<0.05$ (* and †) and $p<0.01$ (¶ and ‡).

were thus selected multiple times, the total number of firms exceeded forty-four. Additionally, because we selected the firms using information from company websites, we were not able to judge technical strength and therapeutic area of focus for a number of these companies.

First, an analysis of research and development targets as their technical strength revealed that there was roughly an even split between 24 firms (55%) advancing biopharmaceutical development and 23 firms (52%) advancing low-molecular-weight compound development. Within biopharmaceuticals, nine firms (20%) were advancing antibodies, followed by seven firms (16%) advancing therapeutic proteins, three firms (7%) advancing nucleic acid, and three firms (7%) advancing vaccines. In terms of distinctive technologies, 30 firms (68%) were confirmed to own distinctive technologies; for example, research results concerning specific proteins associated with diseases, in addition to universal technologies such as DDS (Drug Delivery System), SBDD (Structure-Based Drug Design), and gene analysis technology. However, the remaining one third of the firms did not show any technological advantages. The fact that there are many firms that present no distinctive competitive advantage is considered a problem for Japanese Biotech DDFs.

Next, regarding the therapeutic area of focus, 19 firms (43%) identify cancer as their area of focus and are developing therapeutic drugs using biopharmaceuticals and low-molecular-weight compounds. Many of these firms also identify immunology as an area of focus, which is closely related to cancer. It should be noted that even though pharmaceutical companies think that it is difficult to be involved in the treatment of infectious diseases because satisfaction with existing drugs is high and the anti-infection drug market is small, some firms focus on this therapeutic area as a niche strategy. On the other hand, around one third of the firms did not specify any therapeutic area of focus. Since drugs that address unmet clinical needs are assessed favorably, when the Biotech DDFs form alliances with pharmaceutical companies [12], we are of the opinion that Biotech DDFs should improve their business by being thoroughly aware of the clinical applications.

Finally, 17 firms (39%) were developing other projects outside of the drug development business. This finding lends support to the claim that Motohashi made when analyzing all of the biotech firms—that firms are earning their "daily bread" in low-risk areas [9]. If biotech firms face an environment that does not allow them to concentrate fully on drug research and development, then, that is indeed another problem.

**4) Turnover**

As of Fiscal Year (FY) 2011 or FY2012, 17 of the firms released sales information (mean = 552 million JPY, median = 168 million JPY). Nine of the firms recorded sales in excess of 100 million JPY, while one firm had not recorded sales. Although there was one firm that recorded sales from the pharmaceutical business in excess of five billion JPY, the sales of many of the firms were most likely from non-pharmaceutical business and/or temporary revenues such as milestones from alliances or shared earnings from joint research and development.

**5) Net Profit/Loss**

As of FY2011 or FY2012, 21 of the firms released net profit/loss information (mean = -132 million JPY, median = -124 million JPY). Four of the firms were profitable, but only one of these recorded recurring sales in the pharmaceutical business. The other three firms were considered to become profitable thanks to earnings from businesses other than pharmaceutical business or from milestone revenues from alliances. There were 12 firms with a net loss of 100 million JPY or more; a result of research and development investment that is unique to the drug development business.

**6) Capital**

As of 2012 or 2013, 22 of the firms released their capital information (mean = 642 million JPY, median 100 million JPY). Of the firms that released this information in their company website, we removed from the sample some firms which did not present the date of the capital information. Four of the 22 firms (18%) had capital in excess of 500 million JPY, and they were thus categorized as large companies according to the Japanese Companies Act. Seven of the 22 firms (32%) had capital between 100 to 500 million JPY, and the remaining 11 firms (50%) had capital of 100 million JPY or under. It should be noted that a number of the firms that had capital of 100 million JPY or less have carried out capital reduction plans. While these firms had succeeded in procuring capital, they had not completed a business plan that would cover the period until the next procurement of capital, forcing them to carry out capital reduction plans.

**7) Career Background of President/CEO**

The President/CEO has considerable influence over the development of a business. Therefore, for the President/CEO's career background at the time of the investigation, we examined their previous employment. As a result, 16 firms (36%) were found to be led by former members of pharmaceutical companies, followed by 8 firms (18%) by ones from academia, 6 firms (14%) by ones from non-pharmaceutical companies and 5 firms (11%) by ones from financial sector, while President/CEO's background in 9 firms could not be identified. Since management of Biotech DDFs requires skills such as managerial decision making on drug development, compliance with drug-related regulation, and network building aimed at forming alliances, it is reasonable that a person who has a business experience in a pharmaceutical company plays President/CEO's role.

**8) Size of Workforce**

As of 2012 or 2013, we acquired for 19 firms the following information on workforce size (mean: 26.9 employees, median: 18 employees). Eight firms, the highest percentage, had between 11 and 20 employees, and five firms had between 1 and 10 employees. While the details of the employees' duties have not been ascertained, it is likely that many engage in research and development, and research and development assistance. In addition, there was one firm with more than 200 employees that owned marketed products. Even outside of research and development, this firm requires a large workforce to handle sales and post-marketing safety surveillance, and thereby represents an example of job creation at a biotech firm.

**9) Research and Development Pipeline**

We ascertained the research and development pipeline information from 28 firms. In two of these firms, the latest development stage was market launch; in 18 firms, the latest development stage was clinical development; and for the remaining eight firms the latest development stage was pre-clinical development.

An analysis of 33 compounds undergoing clinical studies revealed that 17 were in Phase 1, 12 were in Phase 2, two were in Phase 3, and two were at the new drug application stage. Thus, most of the products were in a stage of development where their medical efficacy had not been confirmed and therefore had little likelihood of being approved. Eight out of the 33 compounds (25%) had alliance partner companies.

In terms of the therapeutic area, nine of the clinical compounds (27%), the highest percentage, were targeting cancer, six (18%) were targeting orphan diseases, and four (12%) were targeting infectious diseases. Cancer came up most frequently in terms of a firm's therapeutic area of focus and development pipeline. However, considering that cancer is considered as a therapeutic area with the least likelihood of development success [7], clinical programs for cancer treatment do not necessarily guarantee favorable business success. On the other hand, one firm focused on orphan diseases was developing four orphan drugs. In this way, this company has been avoiding direct competition and has succeeded in steadily expanding its business scale.

**10) Patents**

An analysis of the domestic and foreign patent applications and patents granted at the 44 firms sampled confirmed that 41 of the firms had patent applications (Figure 2). In terms of the number of patent applications in a given year, considering the number of years since a business was founded, 12 firms, the highest percentage, made 0.5 to one application per year, and 11 firms made one to two applications per year (Figure 3). Two firms made five applications per year; one had many joint applications with academia, and the other categorized in "JV Business Source Firms" seemed to have research results accumulated before the business was founded.

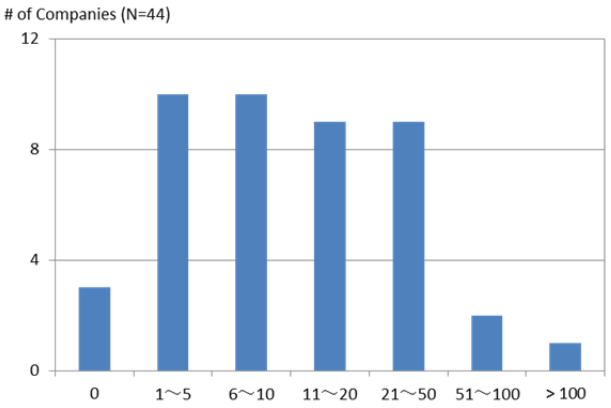


Figure 2. Number of Patent Applications

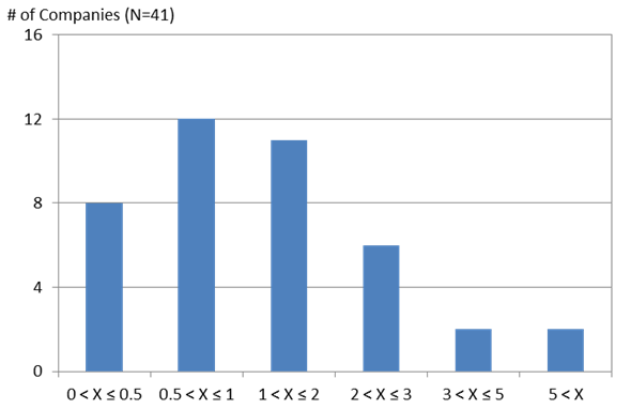


Figure 3. Number of Patent Applications Per Year

In terms of the number of domestic patent granted, 24 firms, the highest percentage, had one to five patents granted (Figure 4). In terms of the rate of domestic patents granted, we analyzed the 31 firms that had made six or more patent applications, to avoid having the data skewed by the unusual characteristics of firms that had very few applications (Figure

5). The results revealed that 16 of the 31 firms (52%), the highest percentage, had a 20-40% success rate.

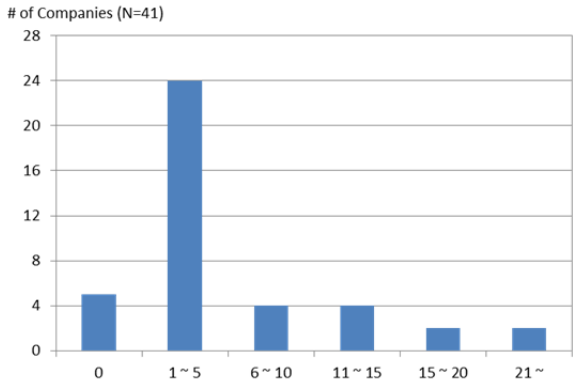


Figure 4. Number of Domestic Patents Granted

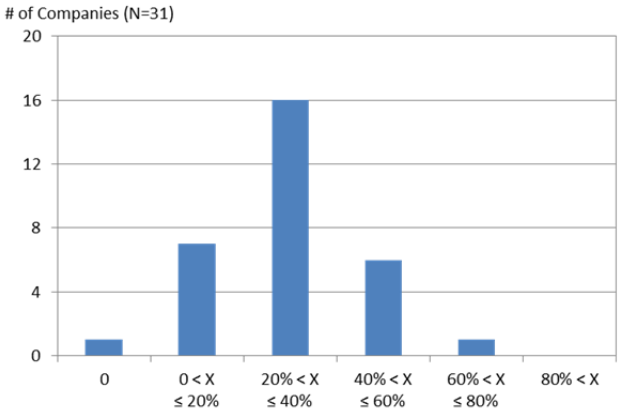


Figure 5. Rate of Domestic Patents Granted

Since the pharmaceutical business can develop on a global level, it is very important to obtain foreign patents. Therefore, we analyzed the firms' foreign patent application situation. This analysis revealed that 34 of the 44 firms had made foreign patent applications (Figure 6); 14 firms had one to five foreign patent applications, and 10 firms had six to ten applications.

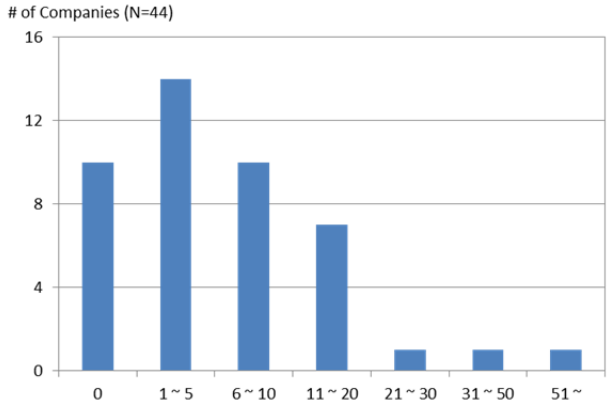


Figure 6. Number of Foreign Patent Applications

We further analyzed the 34 companies that had foreign patent applications in terms of the number of patents granted as well as success rate. The number of firms with one to five patents granted was, as in the case with domestic patents, the highest, at 19 out of 34 (56%) (Figure 7). Fourteen of the 34 firms (41%), the highest percentage, had a 40-60% success rate; a higher success rate compared to domestic patents (Figure 8).

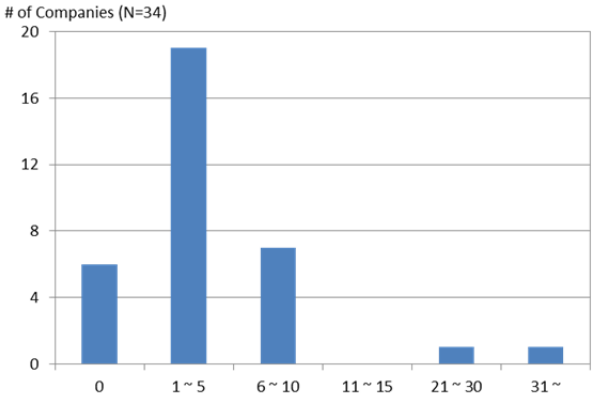


Figure 7. Number of Foreign Patents Granted

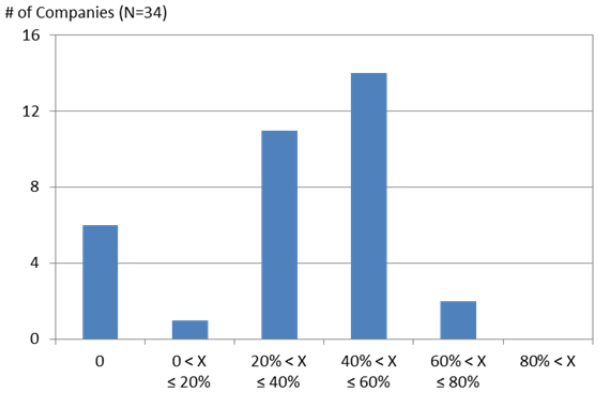


Figure 8. Rate of Foreign Patents Granted

Finally, we analyzed the patent applicants. Of the 41 firms that had patent applications, three firms (7%) made single patent applications in more than 80% of cases, and six (15%) made single patent applications in 60-80% of cases (Figure 9). The figures were lower in the case of joint applications with other firms; only three of the 41 firms (7%) made joint applications with other firms in more than 80% of cases, and only one of the 41 firms (2%) made such applications in 60-80% of cases (Figure 10). These results suggest that many patent applications are made jointly with academia or individuals in academia, and confirm that Japanese Biotech DDFs are reliant on the results of academic research.

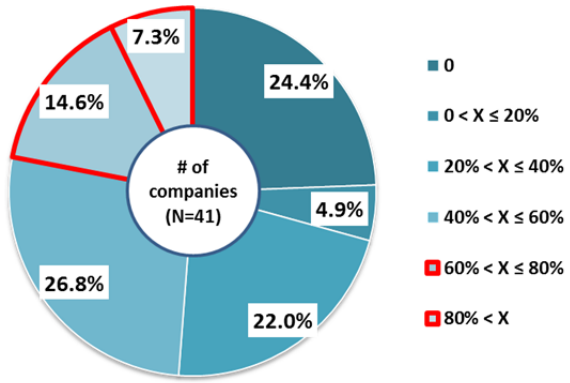


Figure 9. Ratio of Single Applications

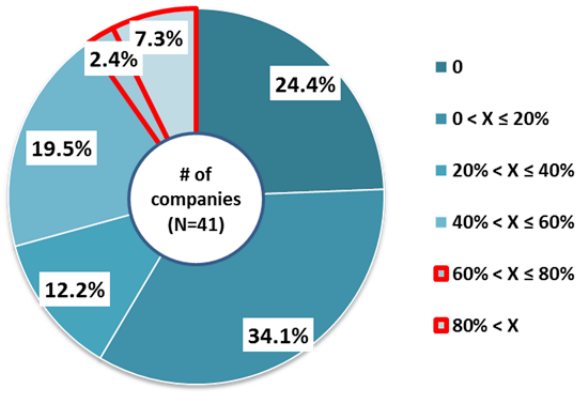


Figure 10. Ratio of Joint Applications with Other Firms

*B. Analysis of the Biotech DDFs' Patents Granted*

The source of the Biotech DDFs' enterprise value lies in their research and development pipeline and patents, which generate profits through marketable products and alliances. Especially, patents ensuring exclusivity are important for pharmaceutical businesses. We thus analyzed the relationship between origin of business and number of patents granted/ patent granted rate (Table 1).

In terms of the number of domestic patents granted, while "JV Business Source Firms" had the highest number, the number of patents granted for "Academia Source Firms" was higher than all firms' mean number. As for the domestic patent granted rate, while "License Source Firms" had the highest rate, the rate of "Academia Source Firms" was the same as all firms' mean rate.

In terms of the number of foreign patents granted, "JV Business Source Firms" scored highly, while the number for "Academia Source Firms" was the same as all firms' mean number. As for the foreign patent granted rate, while "JV Business Source Firms" had the highest rate, "Academia Source Firms" had a granted rate that was above all firms' mean rate.

From these investigation results, we have deduced the following:

1) "Academia Source Firms" have a high proportion of research results that are highly patentable, both domestically and internationally.
2) "JV Business Source Firms" have accumulated a large volume of research results, and thus possess many patent assets.
3) "License Source Firms" have a high rate of domestic patents granted with respect to securing business domestically, but do not have many patents through research results that can lead to granting of foreign patents.
4) Firms considered "Individual or Unidentified Source Firms" have fewer research results that are patentable, either domestically or internationally, than the other category firms.

In relation to this patent analysis, it should be noted that since it takes time for a patent to be granted, the analysis, while making a valid assessment of past research results, should not be considered as representative of the current situation of research results.

## V. DISCUSSION, STUDY LIMITATIONS AND FUTURE PERSPECTIVES

*A. Discussion*

The investigation results covering basic information for the unlisted Biotech DDFs, referenced in section 4.1, revealed that the mean and median turnover, net profit/loss, capital, and size of workforce of the unlisted Biotech DDFs are all higher than those for all biotech firms surveyed by JBA. Considering that the JBA survey included listed firms in its sample, it seems that unlisted Biotech DDFs receive a relatively higher amount of capital investment in Japan—a country where amassing capital is considered difficult and the business scale seems to be large.

However, as we showed in section 4.1.9, there are only 33 clinical compounds owned by 20 firms and, moreover, most of these are in an early development stage where a possibility of success in being approved as a drug is still low [7]. Even though unlisted Biotech DDFs have received a relatively large investment in Japan, most of them are not yielding recurring sales enough to afford research and development activities. In consideration of approximately two billion JPY on average spent for one drug development project from preclinical studies through P-II in which clinical effectiveness is examined [16], the unlisted Biotech DDFs have to continue raising capital to complete clinical studies. Nevertheless, they have faced some difficulties in financing based on our investigation on the capital information in section 4.1.6. We think that the current business base of the unlisted Biotech DDFs is still fragile and thus it will be some time until they can play a role as new drug supply sources.

Regarding a source of enterprise value, the analysis of the granted patents of the unlisted Biotech DDFs referenced in IV.B suggested that "Academia Source Firms" and "JV

Business Source Firms" have obtained new and useful research results and possess domestic and foreign patents. However, since patents are granted based on judgment criteria that varies across countries, and the quality of the patents identified in this study have not been evaluated, we see a need to examine the Forward Citations of the granted patents [8] as a next step. In addition, we believe that, once a Biotech DDF is established, it should have competitive advantage based on its own research outcomes and/or development know-hows, not depending too much on academia research.

*B. Study Limitations*

This study has three limitations.

The first limitation concerns the methodology. This study did not aim to verify a theory or hypothesis. Instead, it aimed to gather a comprehensive collection of information and analyze it. Thus, we did not undertake a quantitative statistical analysis of the data to address any research questions. Furthermore, we only sampled Japanese unlisted Biotech DDFs, so there is also a need to sample firms in other countries for the purpose of a comparative study. We plan to use the results of this research to form a hypothesis, identify a sample for comparative analysis appropriate for verifying the hypothesis, and thereby develop the research further.

The second limitation concerns the coverage of the sampled firms. The study used the JBA's "2012 Survey of Bio-venture Statistics and Trends" as an information source. Among the sample, there were firms that had not updated their website for a long time, as well as some without a website. We plan to augment the sample, as appropriate, by making use of the updated information in the 2013 JBA report released in October 2013, and by using information sources other than the JBA.

The third limitation concerns the public domain information. From many of the financial statements released by the unlisted firms, we could only gain minimal accounting information (for example, turnover and net profit/loss), and, in terms of information on research and development pipelines, not all of this was covered in the commercial database. In the future, based on the database constructed in this study from the public domain information, we will conduct questionnaire surveys and interviews with the firms sampled, thereby raising the accuracy of the information and its comprehensiveness.

*C. Future Perspectives*

The "Japan Revitalization Strategy – Japan Is Back," mentioned at the beginning of this paper, highlights the acceleration of venture businesses as the key to unleash the power of the private sector to its fullest. As the fruits of scientific and technological innovation, pharmaceuticals are products with the highest added value. However, although the government has a high hope for drug discovery/development, this study revealed that the business status of the unlisted Biotech DDFs in Japan is weak.

We plan to conduct an international comparison by forming a JaBit (Japanese Biotech Database) [10], and then referencing ScanBit (Scandinavian Biotech Database) [15], which is a Dedicated Biotech Firms database. To improve the efficiency of the cycle of value creation, especially the generation of new drugs in Japan, we plan to identify the issues faced by Japanese Biotech DDFs and propose policies for addressing them.

## VI. CONCLUSION

In this study, we comprehensively gathered public domain information and created an integrated database to shed light on the business status of Japanese unlisted Biotech DDFs. We then analyzed a source of Biotech DDFs' enterprise value, namely patents, from a perspective of the origin of business, and then this study confirmed that many unlisted Biotech DDFs in Japan are using research results from academia.

Overall, unlisted Biotech DDFs in Japan haven't built solid business base and cannot be considered to have reached a stage yet where they are churning out business results. In order for the Biotech DDFs to achieve good results, they will first need to produce drug candidates that address unmet clinical needs, secure patents that give the business exclusivity on a global level, and work to enrich their research and development pipelines.

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