



ELSEVIER

biotech focus



Patent production is a prerequisite for successful exit of a biopharmaceutical company

Chikako Saotome, saotome.chikako.2z@kyoto-u.ac.jp, Yurie Nakaya and Seiji Abe

Patents are especially important for the business of drug discovery; however, their importance for biopharmaceutical companies has not been revealed quantitatively yet. To examine the correlation between patents and long-term business outcome of biopharmaceutical companies we analyze annual number of patent families and business conditions of 123 public-listed biopharmaceutical companies established from 1990 to 1995 in the USA. Our results show the number of patent families per year correlates well with the business condition: average of the bankruptcy group is significantly smaller than those of the continuing and the merger and acquisitions (M&A) groups. In the M&A by big pharma group, the acquisition cost correlates with the number of annual patent families. However, patentability and strategy of foreign patent application are not different among the groups. Therefore, the productivity of invention is the key factor for success of biopharmaceutical companies.

Introduction

Biopharmaceutical companies have an important role in open innovation in drug discovery. Although intellectual property is important for drug development, there are few studies quantitatively analyzing patents as a success factor of biopharmaceutical companies. Parida *et al.* investigated the numbers of granted patents in the USA, candidates in Phase III and products on the market from 59 American biopharmaceutical companies established between 1992 and 2002, and concluded that there is no correlation between the number of patents and production of drugs or drug candidates in these biotech companies [1]. Deeds *et al.* reported that factors correlating with the amount of capital at the initial public offering (IPO) are location of the

company, the number of products in development and the times of citation on works by scientists of the company and not the number of patents [2]. Lichtenthaler, by contrast, classified 136 European firms into low-, medium- and high-tech firms, and showed that in high-tech firms the return on sales strongly and positively correlates with patent portfolio size [3]. Because a lot of money and time are spent on development of pharmaceutical products, successful biopharmaceutical companies are supposedly more eager to protect their research results as intellectual property to survive in their business. We, therefore, hypothesize that innovative biotech companies file patents more actively, which ultimately increases their value. Here, we take into account several factors to examine the

importance of patents quantitatively in success of biopharmaceutical companies. First, we investigate not only granted US patents but also all patent applications of each company. Next, to eliminate time factor such as time lag between application and grant of patents and years in business, we examine the annual number of patent application to quantitate research efforts of each company. Furthermore, we do not think the amount of IPO an appropriate measure for evaluation for biopharmaceutical companies, because almost no product is marketed at the time of IPO. We, therefore, analyze patent families [a set of patent application(s) from single invention in the USA and abroad] of 123 public-listed biopharmaceutical companies established from 1990 to 1995 in the USA to examine the

importance of patent application for biopharmaceutical company success.

Identification and classification of biopharmaceutical companies for analysis

We searched biopharmaceutical companies in the USA through EDGAR, an online database of the US Securities and Exchange Commission, in five sections with sic codes 2833 (medicinal chemicals and botanical products), 2834 (pharmaceutical preparations), 2835 (*in vitro* and *in vivo* diagnostic substances), 2836 (biological products) and 8731 (services-commercial physical and biological research), and picked up all start-up companies established from 1990 to 1995 for drug discovery in the USA (see Table S1 in Supplementary Material online). We then examined the business state at September 2012 of these 123 companies from their annual reports (form 10-K) from EDGAR and classified their business conditions according to the 'exit' (i.e. bankruptcy, continuing and M&A). Forty-eight companies (39%) continue their business by themselves for about 20 years (the continuing group). Twenty-seven companies (22%) quitted their business or delisted (the bankruptcy group). The remaining 48 companies belong to the M&A group, which is further divided into two. Eighteen companies (15%) were acquired by pharmaceutical companies (the M&A by big pharma group) and 30 companies (24%) were acquired by other biopharmaceutical companies established after 1976 (the M&A by biotech group). For these M&A groups, we checked the M&A cost of each company by press release or newspapers.

Annual patent family number and exit

We searched patent families of each company as of September 2012 through the Thomson Reuters' commercial database: the Derwent Innovations Index. We first counted the total number of patent families of each company by this time. The average and median values of annual numbers of patent families of 123 biopharmaceutical companies are 4.9 and 2.2, respectively (Fig. 1). Among them, only six companies (5%) had no patent family. The bankruptcy group showed the average and median values of 1.6 and 1.4, respectively, and their average value is significantly smaller than those of the continuing and the M&A groups ($P < 0.01$). Among the 27 bankruptcy companies, seven companies (26%) had less than 1.0 annual patent families and 12 (44%) companies had between 1.0 and 2.0 with only eight companies (30%) with more than 2.1. The average and median values of the continuing group are 3.5 and 2.3, respectively.

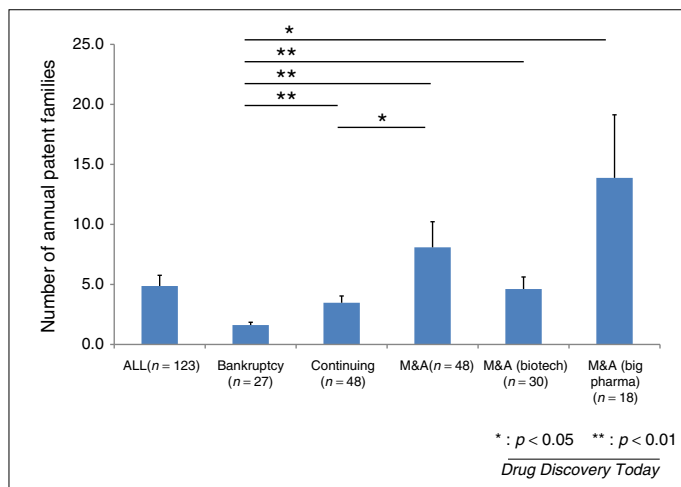


FIGURE 1

Average number of annual patent families.

Among the 48 continuing companies, 15 companies (31%) had less than 1.0 annual patent families, seven companies (15%) between 1.0 and 2.0 and 26 companies (54%) more than 2.1 with 13 companies (27%) producing more than 4.9. The average and median values of the M&A group are 8.1 and 3.6, respectively. Among the M&A group, the M&A by big pharma group has higher average (13.9) and median (4.4) values than those of the M&A by biotech group (4.6 and 2.4, respectively), and the average value of the M&A by big pharma is significantly higher than those of the bankruptcy group ($P < 0.05$). Among the 30 M&A by biotech companies, four companies (13%) had less than 1.0 annual patent families, ten companies (33%) between 1.0 and 2.0 and 16 companies (53%) more than 2.1 with eight companies (27%) producing more than 4.9. In the 18 M&A by big pharma companies, only three companies (17%) had less than 1.0 annual patent families, 13 companies (72%) more than 2.1 and eight companies (44%) producing more than 4.9. Companies producing the highest and the second-highest number of annual patent families are Millennium Pharmaceuticals (81.5) and Human Genome Science (60.9), respectively, both of which belong to the M&A by big pharma group.

Patent family analysis

We next analyzed in more detail the patent families in terms of the quality of patent and foreign patent application (Table 1). The ratio of granted patent in any country, which we evaluated as a measure of the quality of invention, ranged from 60% to 70% and, although the values of the M&A by biotech group are higher than those of the bankruptcy group and the continuing group ($P < 0.05$ and $P < 0.01$, re-

spectively), the difference between their percentage values was not big. We next analyzed their foreign patent applications. Because Europe, USA and Japan occupy about 70% of the drug market in the world according to report by IMS Health <http://www.imshealth.com/files/web/Corporate/News/Top-Line%20Market%20Data/Global%20Prescription%20Sales%20Information%20World%20figures%20by%20Region%202015-2019.pdf>, we examined the percentage of their Patent Cooperation Treaty (PCT) application to the World Intellectual Property Organization (WIPO) and the percentage and number of applications to European, US and Japanese patent offices in addition to WIPO as the 'tripod patent family'. These analyses have revealed that there is no difference in the percentage of the PCT applications, EU applications and the tripod applications and the average number of filed countries. However, the annual numbers of tripod patent families, either total or granted, of the M&A group is significantly more than those of the other two groups. These findings indicate that all the groups adopted the same patent policy but the number of patents that matter was different among the groups.

Correlation between patent number and the M&A cost

We finally analyzed the annual number of patent families and the acquisition cost of each company in the M&A groups (Figs 2,3). We identified acquisition costs of 28 out of 30 companies in the M&A by biotech group, and found that the average cost of acquisition of these companies was US\$477 million. The analysis found no correlation between the acquisition cost and the annual patent families number ($r = 0.0$). We identified all acquisition costs in the M&A by big

TABLE 1
Analysis of patent family

	Bankruptcy (n = 27)	Continuing (n = 48)	M&A (n = 48)	M&A by big pharma (n = 18)	M&A by biotech (n = 30)
Granted patent (%) ^a	59.7 ± 28.7	53.7 ± 14.3	70.6 ± 17.8 ^c	64.3 ± 18.3 ^d	74.6 ± 16.6 ^{e,c}
PCT (%) ^a	82.3 ± 16.7	83.7 ± 14.4	73.7 ± 23.8 ^d	78.7 ± 15.0	70.6 ± 27.7 ^d
EU (%) ^a	57.9 ± 15.6	60.1 ± 17.7	56.0 ± 18.7	57.0 ± 15.0	55.4 ± 21.0
Country number ^a	3.7 ± 1.6	3.8 ± 1.2	3.7 ± 1.4	3.8 ± 1.3	3.6 ± 1.4
Tripod patent (%) ^a	35.9 ± 21.8	42.5 ± 16.6	38.7 ± 15.9	38.4 ± 12.4	38.9 ± 18.0
Annual tripod patent families	0.6 ± 0.5	1.3 ± 1.6 ^b	2.4 ± 3.2 ^{b,d}	3.8 ± 4.5 ^{b,d}	1.6 ± 1.8 ^b
Annual tripod patent families with granted patent	0.5 ± 0.4	0.9 ± 1.0 ^b	2.0 ± 2.4 ^{b,c}	3.0 ± 3.3 ^{b,d}	1.4 ± 1.6 ^b
Annual tripod patent families with more than five countries	0.4 ± 0.3	0.8 ± 0.9 ^b	1.2 ± 1.3 ^b	1.8 ± 1.7 ^{b,d}	0.8 ± 0.9 ^e
Annual tripod patent families with more than ten countries	0.2 ± 0.2	0.3 ± 0.3	0.4 ± 0.7 ^e	0.6 ± 0.8 ^e	0.3 ± 0.6

^a Calculated without companies with no patent family (bankruptcy: 1; continuing: 4; M&A by biotech: 1).

^b Significance level is less than 1% compared to the bankruptcy group.

^c Significance level is less than 1% compared to the continuing group.

^d Significance level is less than 5% compared to the continuing group.

^e Significance level is less than 5% compared to the bankruptcy group.

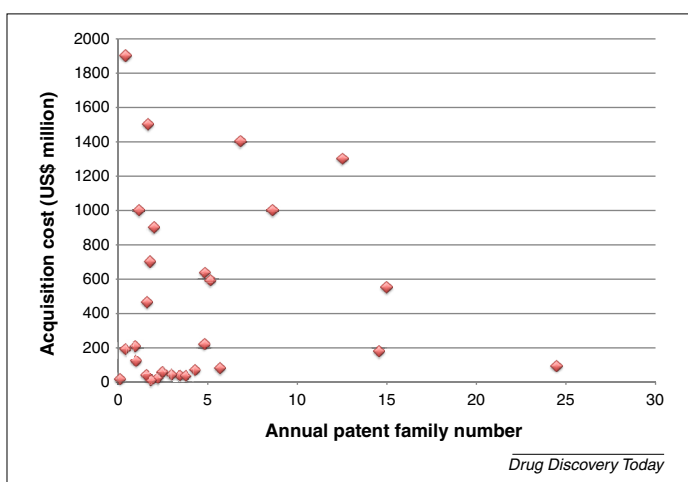


FIGURE 2
Acquisition cost versus annual patent families number in the M&A by biotech group.

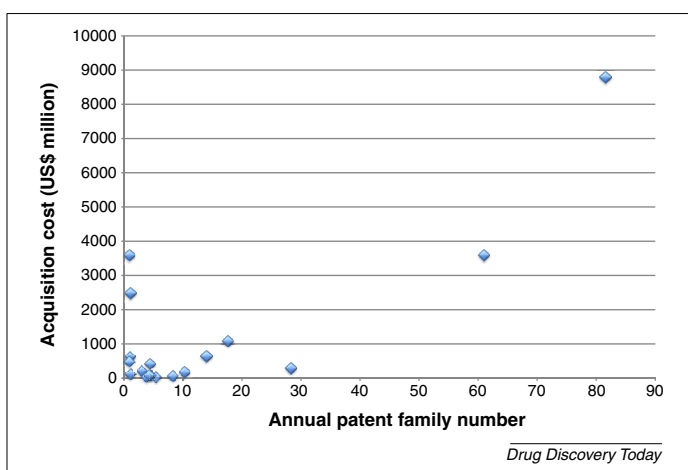


FIGURE 3
Acquisition cost versus annual patent families number in the M&A by big pharma group.

pharma group and found that the average cost was more expensive (US\$1283 million) than that of M&A by biotech group. In contrast to the M&A by biotech group, modest correlation ($r = 0.80$) was found between the cost and the annual number of patent families in the M&A by big pharma group. These results suggest that pharmaceutical companies hold high value on the intellectual property of a biopharmaceutical company in their evaluation. Both groups show no correlation between acquisition cost and acquisition year (data not shown).

Discussion

Here we examined the importance of intellectual property management for biopharmaceutical companies by investigating all patent families (inventions) of 123 public-listed biopharmaceutical companies established about 20 years ago. Our results show that the number of patent families per year correlates well with the business condition of biopharmaceutical companies and the value of M&A by big pharma, although patentability and strategy of foreign patent application are not different among the groups. Therefore, the productivity of invention is the key factor for success of biopharmaceutical companies.

A question is why the annual patent families number correlates with the business condition of biopharmaceutical companies in our study despite previous reports that the number of patents was correlated neither with production of drug [1] nor the value at the IPO [2]. First, even the bankruptcy companies among the biopharmaceutical companies in our analysis had value for investors at the time of IPO. Such value was probably based on location

of the company, the number of products in development and the times of citation on works by scientists of the company and not the number of patents as reported by Deeds *et al.* [2].

However, they had not developed drugs or technologies of their own since then and failed to make an invention. As a consequence, they could have lost competitiveness and the value for investors and pharmaceutical companies, and they went bankrupt because they failed to get funding for drug development. By contrast, innovative biopharmaceutical companies apparently have more drugs and technologies of their own. They, therefore, became the target for acquisition by pharmaceutical companies that want to expand their drug pipelines or introduce new technologies. Stuart *et al.* investigated alliance activities of biotech companies with universities (upstream alliances) as well as pharmaceutical companies (downstream alliances) and found that many young biotechnology firms act as intermediaries in such tripartite alliance chains but the positive relationship between in-licenses from upstream alliance and revenue generation from downstream alliance attenuates in matured biotech companies [4]. Their results support the importance for biopharmaceutical companies to conduct original research in house. Pharmaceutical companies could place more value on actual drugs or drug candidates and/or new technology to generate them filed in patents than biotech companies, because of correlation between annual patent families number and acquisition cost in the M&A by big pharma. Furthermore, having their own patents reduces the risk for patent infringement or licenses. Therefore, patent production is a prerequisite for being continuing or bought by M&A of biopharmaceutical companies. Even though the annual patent families number of the M&A by biotech group is significantly more than that of the bankruptcy and the continuing groups, it has

no correlation with M&A cost. There could be difference of aim and evaluation for M&A between big pharma and biotech companies.

Which factor of inventiveness determines the outcome of biopharmaceutical companies that have only limited resource at their beginning? Our research showed that companies producing the highest and the second-highest number of annual patent families are Millennium Pharmaceuticals and Human Genome Science. They conducted research on identification of new causative genes in various human diseases for development of new drugs. We suggest that conducting drug discovery research based on new technology from an early phase of its development results in many inventions. Active patent application policy combined with such research activity is also important for producing many inventions.

Concluding remarks

Our results clearly show that the continuing group and M&A groups have filed significantly more patents per year than the bankrupted biopharmaceutical companies. M&A companies filed plenty of patents each year, and their acquisition cost increased as they filed more patents. M&A groups also had a slightly higher ratio of granted patents. Therefore, capability of making an invention is crucial for biotech companies. Source of creation of invention and success factor of biopharmaceutical companies are factors that will be identified in future by analysis of a claim of patent application, business model, number of products and alliance.

Conflicts of interest

The authors declare no conflicts of interest relevant to the subject matter discussed in the manuscript.

Acknowledgments

The authors would like to thank all of the

members of the Management Technology and Intellectual Property Department of the Kyoto University Graduate School of Medicine for their valuable comments and suggestions. We also sincerely appreciate Prof Shuh Narumiya at the Kyoto University Graduate School of Medicine for support and encouragement to write the paper. This work was supported by a research grant from the Association for Technological Excellence Promoting Innovative Advances (TEPIA) in Japan and by a Grant-in Aid for Scientific Research (No. 00447963) to CS from The Ministry of Education, Culture, Sports, Science and Technology (MEXT) in Japan.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drudis.2015.12.005>.

References

- 1 Parida, D.K. *et al.* (2008) How many patents does a biopharmaceutical company need? *Nat. Biotechnol.* 26, 763–766
- 2 Deeds, D.L. *et al.* (1997) The impact of firm-specific capabilities on the amount of capital raised in an initial public offering: evidence from the biotechnology industry. *J. Bus. Venturing* 12, 31–46
- 3 Lichtenthaler, U. (2009) The role of corporate technology strategy and patent portfolios in low-, medium- and high-technology firms. *Res. Policy* 38, 559–569
- 4 Stuart, T.E. *et al.* (2007) Vertical alliance networks: the case of university–biotechnology–pharmaceutical alliance chains. *Res. Policy* 36, 477–498

Chikako Saotome*
Yurie Nakaya
Seiji Abe

Kyoto University Graduate School of Medicine, 53 Kawaharacho, Shogoin, Sakyo, Kyoto 606-8507, Japan

*Corresponding author.