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

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A teaser: Long-term business outcome of biopharmaceutical companies, such as M&A and bankruptcy, correlates well with the number of patent families per year.

#### Abstract

Patent is especially important for the business of drug discovery, however, its importance for biopharmaceutical companies has not 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 United States. Our results show the number of patent families per year correlates well with the business condition, that is average of the Bankruptcy group is significantly smaller than those of the Continuing and the 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.

Biopharmaceutical companies play an important role in open innovation in drug discovery. Though 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 the United States (US) patents, candidates in phase 3 and products in market in 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/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, on the other hand, 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]. Since a lot of money and time are spent for development of pharmaceutical products, successful biopharmaceutical companies are supposed 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

quantitatively examine the importance of patents 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 in market at the time of IPO. We, therefore, analyze patent families (a set of patent application(s) from single invention in the US and abroad) of 123 public-listed biopharmaceutical companies established from 1990 to 1995 in the US to examine the importance of patent application for biopharmaceutical companies' success.

#### Identification and classification of biopharmaceutical companies for analysis

We searched biopharmaceutical companies in the US through the EDGAR, an on line database of the US Securities and Exchange Commission, in five sections with sic codes, 2833 (medicinal chemicals & botanical products), 2834 (pharmaceutical preparations), 2835 (in vitro & vivo diagnostic substances), 2836 (biological products), and 8731 (services-commercial physical & biological research), and picked up all start-up companies established from 1990 to 1995 for drug discovery in the US (Supplementary Table 1). 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 twenty years (the Continuing group). Twenty-seven companies (22%) quitted their business or delisted (the Bankruptcy group). The rest 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 families 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 6 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, 7 companies (26%) had less than 1.0. annual patent families, and 12 (44%) companies between 1.0 and 2.0 with only 8 companies (30%) more than 2.1. The average and median values of the Continuing group are 3.5 and 2.3 respectively. Among the 48 Continuing companies, 15 companies (31%) had less than 1.0. annual patent families, 7 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, 4 companies (13%) had less than 1.0. annual patent families, 10 companies (33%) between 1.0 and 2.0, and 16 companies (53%) more than 2.1 with 8 companies (27%) producing more than 4.9. In the 18 M&A by Big Pharma companies, only 3 companies (17%) had less than 1.0. annual patent families, 13 companies (72%) more than 2.1 with 8 companies (44%) producing more than 4.9. Companies producing the highest and the second highest number of annual patent families are the Millennium Pharmaceuticals, Inc. (81.5) and the Human Genome Science, Inc. (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 term 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 is higher than that of the Bankruptcy group and the Continuing group (P<0.05 and P<0.01, respectively), the difference

between their % values was not big. We next analyzed their foreign patent applications. Since Europe, US and Japan occupy about 70% of the drug market in the world according to report by IMS Health (see: http://www.imshealth.com/ deployedfiles/imshealth/Global/Content/Corporate/Press%20Room/Total World Pharm a Market Topline metrics 2012-17 regions.pdf), we examined the percentage of their PCT application to the World Intellectual Property Organization (WIPO), and the percentage and number of applications to European, US and Japan patent office 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 matters 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 \$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 Pharma group, and found that the average cost was more expensive (\$1,283 million) than that of M&A by Biotech group. On the contrary 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 put much value on intellectual property of a biopharmaceutical company in their evaluation. Both groups show no correlation between acquisition cost and acquisition cost and acquisition year (data not shown).

#### Discussion

Here we examined the importance of intellectual property management for business of 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 patent was correlated neither with production of drug [1] nor the value at the IPO [2]. Firstly, even the Bankruptcy companies among the biopharmaceutical companies in our analysis had had the 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 may have lost competitiveness and the value for investors and pharmaceutical companies, and they went bankrupt because they failed to get fund for drug development. On the other hand, 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 result supports the importance for biopharmaceutical companies to conduct original research in house. Pharmaceutical companies may place more value on actual drugs/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 others' patent infringement or license. 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 may be difference of aim and evaluation way for M&A between big pharma and biotech company.

Then, what 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 the Millennium Pharmaceuticals, Inc. and the Human Genome Science, Inc. 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 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.

# Conclusion

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 a plenty of patents a year, and their acquisition cost increased as they filed more patents. M&A groups also slightly higher than the ratio of granted patent. Therefore, capability of making an invention is crucial for biotech companies. Source of creation of invention and success factor of biopharmaceutical companies will be identified in future by analysis of a claim of patent application, business model, number of products and alliance.

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# **Conflict of interest**

All authors declare no conflict of interest relevant to the subject matter discussed in the manuscript.

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# Legends for figures

Fig. 1 Average of annual patent families number

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

Fig. 3 Acquisition cost versus annual patent families number in the M&A by Big Pharma group

	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	59.7±28.7	53.7±14.3	70.6±17.8 <sup>##</sup>	64.3±18.3 <sup>#</sup>	74.6±16.6*, ##
(%) <sup>a)</sup>					
PCT (%) a)	82.3±16.7	83.7±14.4	73.7±23.8 <sup>#</sup>	78.7±15.0	70.6±27.7 <sup>#</sup>
EU (%) <sup>a)</sup>	57.9±15.6	60.1±17.7	56.0±18.7	57.0±15.0	55.4±21.0
Country	3.7±1.6	3.8±1.2	3.7±1.4	3.8±1.3	3.6±1.4
number <sup>a)</sup>					
Tripod patent	35.9±21.8	42.5±16.6	38.7±15.9	38.4±12.4	38.9±18.0
(%) <sup>a)</sup>					
Annual tripod	0.6±0.5	1.3±1.6**	2.4±3.2** <sup>, #</sup>	3.8±4.5** <sup>, #</sup>	1.6±1.8**
patent families					
Annual tripod	0.5±0.4	0.9±1.0**	2.0±2.4** <sup>,##</sup>	3.0±3.3** <sup>,#</sup>	1.4±1.6**
patent families					
with granted					
patent					
Annual tripod	0.4±0.3	0.8±0.9**	1.2±1.3**	1.8±1.7** <sup>,#</sup>	0.8±0.9*
patent families					
with more 5					
countries					
Annual tripod	0.2±0.2	0.3±0.3	0.4±0.7*	0.6±0.8*	0.3±0.6
patent families					
with more 10					
countries					

Table 1. Analysis of Patent Family

a) Calculated without companies with no patent family (Bankruptcy: 1, Continuing: 4, M&A by Biotech :1)

\* Significance level is less than 5% compared to the Bankruptcy group.

\*\* Significance level is less than 1% compared to the Bankruptcy group.

<sup>#</sup>Significance level is less than 5% compared to the Continuing group.

<sup>##</sup>Significance level is less than 1% compared to the Continuing group.

# Supplementary Table 1: 125 Biopharmaceutical Companies established from 1990 to 1995 in US

Company name	Year of	Exit	Acquisition Cost	Annual
	Formation		(million dollars)	Patent
				Families
				Number
3 DIMENSIONAL	1993	M&A by	88	8.2
PHARMACEUTICALS INC		Big Pharm		
ACADIA	1993	Continuing		4.2
PHARMACEUTICALS INC				
ACORDA THERAPEUTICS	1995	Continuing		2.6
INC				
ACUSPHERE INC	1993	Bankruptcy		1.9
ADOLOR CORP	1993	M&A by	221	4.8
		Biotech		
AEOLUS	1994	Continuing		0.4
PHARMACEUTICASL INC				
AGENUS INC	1994	Continuing		0.1
ALBANY MOLECULAR	1991	Continuing		3.5
RESEARCH INC				
ALEXION	1992	Continuing		5.6
PHARMACEUTICALS INC				
ALGOS PHARMACEUTICAL	1992	M&A by		2.0
CORP		Biotech		
ALLOS THERAPEUTICS INC	1992	M&A by	206	1.0
		Biotech		
ANADYS	1992	M&A by	230	2.9
PHARMACEUTICALS INC		Big Pharm		
ANDRX CORP	1992	M&A by	1900	0.4
		Biotech		
ANTEX BIOLOGICS INC	1991	Bankruptcy		2.4
ARCA BIOPHARMA INC	1992	Continuing		0.5

ARDEA BIOSCIENCES INC	1994	Continuing		2.1
ARIAD PHARMACEUTICALS	1991	Continuing		5.1
INC				
ARQULE INC	1993	Continuing		5.2
ATHEROGENICS INC	1993	Bankruptcy		2.5
ATHERSYS INC	1995	Continuing		1.8
AURORA BIOSCIENCES	1995	M&A by	592	5.2
CORP		Biotech		
AVAX TECHNOLOGIES INC	1990	Bankruptcy		0.1
AVICENA INC	1993	Bankruptcy		1.3
AVIGEN INC.	1992	M&A by	37	3.5
		Biotech		
AVIRON INC	1992	M&A by	1500	1.7
		Biotech		
BIODELIVERY SCIENCES	1995	Continuing		1.0
INTERNATIONAL INC				
BIOSPECIFICS	1990	Continuing		0.0
TECHNOLOGIES CORP				
BIOTRANSPLANT INC	1990	Bankruptcy		2.2
CELL PATHWAYS INC	1990	M&A by	80	5.7
		Biotech		
CELL THERAPEUTICS INC	1992	Continuing		6.9
CENTAUR	1992	Bankruptcy		2.9
PHARMACEUTICALS INC				
COLLATERAL	1995	M&A by	140	1.0
THERAPEUTICS INC		Big Pharm		
CONNETICS CORP	1993	M&A by	640	0.9
		Big Pharm		
CORIXA CORP	1994	M&A by	300	28.2
		Big Pharm		
COULTER	1995	M&A by	900	2.0
PHARMACEUTICALS INC		Biotech		

CUBIST PHARMACEUTICALS	1992	Continuing		2.8
INC				
CURAGEN CORP	1993	M&A by	93.5	24.5
		Biotech		
CV THERAPEUTICS INC	1990	M&A by	1400	6.8
		Biotech		
DENDREON CORP	1992	Continuing		2.9
DEPOMED INC	1995	Continuing		1.9
DIATIDE INC	1990	M&A by	100	4.4
		Big Pharm		
DISCOVERY LABORATORIES	1992	Continuing		0.5
INC				
ELECTROPHARMACOLOGY	1990	Bankruptcy		0.2
INC				
ENDOCYTE INC	1995	Continuing		1.6
ENTREMED INC	1991	Continuing		2.4
EPICEPT CORP	1993	Continuing		0.5
EPIGEN INC	1991	Bankruptcy		0.4
ERGO SCIENCE CORP	1990	Bankruptcy		1.4
ESSENTIAL THERAPEUTICS	1992	Bankruptcy		1.8
INC				
EUTHYMICS BIOSCIENCE	1995	Bankruptcy		1.6
INC				
EXELIXIS INC	1994	Continuing		17.6
GELTEX	1992	M&A by	1000	8.6
PHARMACEUTICALS INC		Biotech		
GENEMEDICINE INC	1992	M&A by	42	3.0
		Biotech		
GENETHERA INC.	1995	Continuing		0.0
GENVEC INC	1992	Continuing		4.1
GERON CORP	1990	Continuing		6.8
GLYCOGENESYS INC	1992	Bankruptcy		0.7

GUIFORD	1993	M&A by	177.5	14.6
PHARMACEUTICALS INC		Biotech		
HARBOR BIOSCIENCES INC	1994	Bankruptcy		1.1
HUMAN GENOME SCIENCES	1992	M&A by	3600	60.9
INC		Big Pharm		
ICAGEN INC	1992	M&A by	56	3.7
		Big Pharm		
ILEX ONCOLOGY INC	1993	M&A by	1000	1.2
		Biotech		
INCYTE CORP	1991	Continuing		14.8
INFINITY	1995	Continuing		2.3
PHARMACEUTICALS INC				
INHIBITEX INC	1994	M&A by	2500	1.1
		Big Pharm		
INKINE PHARMACEUTICAL	1993	M&A by	190	0.4
CO INC		Biotech		
INSPIRE	1993	M&A by	430	4.3
PHARMACEUTICALS INC		Big Pharm		
INTROGEN THERAPEUTICS	1993	Bankruptcy		2.3
INC				
ISTA PHARMACEUTICALS	1992	M&A by	500	0.8
INC		Big Pharm		
KING PHARMACEUTICALS	1993	M&A by	3600	0.8
INC		Big Pharm		
KOSAN BIOSCIENCES INC	1995	M&A by	190	10.2
		Big Pharm		
LEUKOSITE INC	1992	M&A by	635	4.9
		Biotech		
LEXICON	1995	Continuing		6.3
PHARMACEUTICALS, INC				
LXR BIOTECHNOLOGY INC	1992	Bankruptcy		3.1
MANNKIND CORP	1991	Continuing		4.6

MEDIVATION INC	1995	Continuing		0.5
MILLENNIUM	1993	M&A by	8800	81.5
PHARMACEUTICALS INC		Big Pharm		
MINRAD INTERNATIONAL,	1994	M&A by	40	1.6
INC		Biotech		
MONOGRAM BIOSCIENCES	1995	M&A by	106.7	4.2
INC		Big Pharm		
MYRIAD GENETICS INC	1991	Continuing		10.5
NEKTAR THERAPEUTICS	1990	Continuing		13.8
NEOPHARM INC	1990	Bankruptcy		2.3
NEUROCRINE BIOSCIENCES	1992	Continuing		5.2
INC				
NEXSTAR	1991	M&A by	550	15.0
PHARMACEUTICALS INC		Biotech		
NITROMED INC	1992	Bankruptcy		5.8
OMEROS CORP	1994	Continuing		2.7
ONCOGENEX	1991	Continuing		0.0
PHARMACEUTICALS INC				
ONYX PHARMACEUTICALS	1992	Continuing		3.2
INC				
OPKO HEALTH INC	1991	Continuing		0.7
ORAVAX INC	1990	M&A by	20	2.2
		Biotech		
ORE PHARMACEUTICAL	1994	Bankruptcy		1.3
HOLDINGS INC				
ORPHAN MEDICAL INC	1994	M&A by	122.6	1.0
		Biotech		
PANACOS	1992	Bankruptcy		1.6
PHARMACEUTICALS INC				
PATHOGENESIS CORP	1991	M&A by	700	1.8
		Biotech		
PHARMACYCLICS INC	1991	Continuing		5.6

PHARMAPRINT INC	1994	Bankruptcy		1.3
PRAECIS	1993	M&A by	54.8	5.3
PHARMACEUTICALS INC		Big Pharm		
PROGENITOR INC	1992	Bankruptcy		2.0
QUESTCOR	1992	Continuing		0.6
PHARMACEUTICALS INC				
SANGAMO BIOSCIENCES	1995	Continuing		7.0
INC				
SCICLONE	1990	Continuing		2.0
PHARMACEUTICALS INC				
SIGA TECHNOLOGIES INC	1995	Continuing		1.7
SIRNA THERAPEUTICS INC	1992	M&A by	1100	17.5
		Big Pharm		
SPARTA PHARMACEUTICALS	1990	M&A by		0.0
INC		Biotech		
SUGEN INC	1991	M&A by	650	13.9
		Big Pharm		
SUNPHARM CORPORATION	1990	M&A by	16.5	0.1
		Biotech		
SYNERGY	1992	Continuing		0.5
PHARMACEUTICALS INC				
TAPESTRY	1991	Bankruptcy		1.2
PHARMACEUTICALS INC				
TG THERAPEUTICS INC	1993	Continuing		0.0
TITAN PHARMACEUTICALS	1992	Continuing		0.7
INC				
TRANSCEND THERAPEUTICS	1992	M&A by	8	1.9
INC		Biotech		
TREGA BIOSCIENCES INC	1991	M&A by	35	3.8
		Biotech		
TRIANGLE	1995	M&A by	464	1.6
PHARMACEUTICALS INC		Biotech		

TRINITY MEDICAL GROUP	1995	Bankruptcy		0.0
INC				
TULARIK INC	1991	M&A by	1300	12.5
		Biotech		
URIGEN	1992	Continuing		0.1
PHARMACEUTICALS INC				
VARIAGENICS INC	1992	M&A by	55.9	2.5
		Biotech		
VION PHARMACEUTICALS	1992	Bankruptcy		1.2
INC				
VIRAL GENETICS INC	1995	Bankruptcy		0.5
VIROPHARMA INC	1994	Continuing		2.3
VIRUS RESEARCH	1991	M&A by	70	4.3
INSTITUTE INC		Biotech		
VIVUS INC	1991	Continuing		2.0
XECHEM INTERNATIONAL	1994	Bankruptcy		0.5
INC				



\* : P<0.05 \*\* : P<0.01



