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Entrepreneurial patent management in pharmaceutical startups

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Startups fill an increasingly important role as innovators in the pharmaceutical industry, and patenting is typically central to their success. This article aims to explore patent management in pharmaceutical startups. The results show that startups need to deal with several challenges related to patenting and an 'entrepreneurial' approach to patent management is called for. Resource constraints, venture capital provision, exits and other conditions and events must be readily considered in the patent management process to build a successful pharmaceutical venture, something that could benefit the pharmaceutical industry as a whole.

Introduction

Pharmaceutical startups have an important role in pharmaceutical industry innovation. Incumbent firms nowadays struggle to develop new blockbuster drugs [1] and industry reports point at escalating R&D expenditures, amounting to roughly US\$140 billion per year (<http://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/>), in parallel with decreasing numbers of innovations (T. Hedner, PhD thesis, Linköping University, 2012). However, small firms have continued to innovate and develop new drugs. This situation has called for increased interaction between large established firms, with their capabilities in marketing and production, and small innovative startups (Ibid.), and a model for innovation that is more 'open' (<http://www.forbes.com/sites/henrychesbrough/2011/04/25/pharmaceutical-innovation-hits-the-wall-how-open-innovation-can-help/>). Open innovation is commonly defined as an innovation paradigm 'that assumes

that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as firms look to advance their technology' [2].

Contrary to what one might think, patents play an important part in open innovation. Thus, open innovation is not about abolishing patenting. Instead, patents are used to govern the interaction between multiple actors in open innovation, for example by defining and protecting the technologies that are related to a large firm's acquisition of a startup. Therefore, patents and other intellectual property rights must be carefully managed, especially in pharmaceutical startups. This is not only to provide sufficient returns to the individual firms but also to increase the potential of the pharmaceutical innovation system as a whole.

In an interesting article in *Drug Discovery Today*, Bader *et al.* presented a patent lifecycle management model, providing guidance for management on how to deal with patenting and

related matters throughout the lifecycle of a product within the pharmaceutical industry [3]. This model was by and large based upon and designed for large pharmaceutical enterprises. However, small firms, and especially startups, have significantly different characteristics to large firms, and the importance of, motives for and strategies of patenting are different [4]. Because pharmaceutical startups take an increasingly important role as innovators in the industry, this article aims to explore patent management in pharmaceutical startups to guide the future creations and management of patent portfolios.

Previous research has indicated that small firms in general have lower propensities to patent³ than large firms [4,5]. An important reason for this is that small firms have limited resources for applying for, monitoring and

³ The propensity to patent is typically defined as the probability to patent a patentable invention.

enforcing patents [4]. In general, small technology-based firms often lack financial capital [6], and patenting is not always prioritized. However, in the pharmaceutical industry, with its large investments and long R&D times, patents are of paramount importance to recover sufficient returns from investments in R&D [7], and the propensity to patent is high [5]. In total, far more than two million patent applications are filed each year worldwide, and the area of pharmaceuticals accounts for roughly 3.6% of these (as of 2012, the most recent year with available data at the technology level) [8]. Although there are relatively few patentable inventions within the pharmaceutical industry, each one of these is typically patented in a large number of nations and some can be worth billions of US\$ each year [9].

The PULS network

The article is based upon an in-depth study of the Swedish pharmaceutical partnership network PULS, the largest private life-science incubator in Sweden, including several cases of pharmaceutical startups such as Adenovir Pharma, DuoCort and Laccure. PULS evaluates, develops and invests in early-stage pharmaceutical projects, and contributes with scientific and business development until exit. The empirical data were collected through interviews, documents and observations. One of the authors here is an active member of the network, enabling rich data and in-depth understanding of the cases. PULS started as a bridge between university research and entrepreneurial development and commercialization of research results, and the partnership currently consists of roughly 40 partners (individuals including researchers, entrepreneurs, etc.). It has in total raised about 480 million SEK⁴ since its start in 2002, and divested projects for more than 1.2 billion SEK in total deal value. So far more than 350 million SEK has been brought back to the investors as dividend. Thus, PULS must be considered a successful enterprise; managing to develop several pharmaceutical innovations and to provide positive financial returns.

Two important pillars of the PULS business model, guiding which projects that are taken on, are that there must be a good patent or patentability situation in the project and that there should be a clear market for the future product and for exiting the project, primarily through a divestment. There is 'a focus on an exit strategy

TABLE 1
PULS projects.

Name	Area	Status
AcuCort	Acute allergic reactions	Ongoing
Adenovir Pharma	Eye infections	Ongoing
Glactone Pharma	Prostate cancer	Ongoing
Laccure	Bacterial vaginosis	Ongoing
Oncorena	Renal cancer	Ongoing
Ambria Dermatology	Dermatology	Exit 2009: milestones up to 32 million SEK
DuoCort	Adrenal insufficiency	Exit 2011: milestones up to 1080 million SEK
LIDDS	Various cancers	Exit (IPO) 2014: market cap 113 million SEK as of 2015
Pharmapnea	Sleeping disorders	Discontinued

from the start' (<http://www.pulsinvest.se/about-puls/advantages/>). This model combines aspects of entrepreneurial causation and effectuation, with a focus on addressing existent market needs (causation) while utilizing a limited and controllable amount of resources (effectuation) [10]. Nine projects have been developed within the network, out of which three have been exited (Table 1). The discussion here is based on these projects to exemplify patent management in pharmaceutical startups.

Patent management in PULS

As described above, a number of factors make patent management in startups different from that in large firms. The most prominent one identified in this research is the lack of financial resources, which impacts how pharmaceutical startups work with the timing of patent filings:

*"The strategy [of PULS] is basically to file for patents as late as possible, while considering and avoiding the risk that someone else steals the idea. [...] A common mistake among many small firms is that they file for patents too early, and suddenly they sit there with huge patent costs that they can't handle. We have this type of firms approaching us here at PULS now and then. They have had an idea and filed for a patent, and then the patent process continues, and suddenly the costs start increasing when they enter the national phase [of patenting]. They haven't expected this and they have no possibilities to cover the costs [at that early stage]."*⁵

Another interviewee explains that for pharmaceutical startups the amount of money spent on patenting is substantial, and that they "have to try and delay these costs as much as possible because it affects [their] liquidity". In the meantime, they need to rely on secrecy to protect the inventions from imitation while simultaneously keeping the option to patent later (which requires novelty). Although the delay of patenting limits costs, it also extends the patent protection time, which is another important reason to patent late:

"The strategy is to try to delay patenting as much as possible, partly to get as long patent protection as possible, but also to avoid very large patent costs initially. [...] It takes 10–15 years to get a product on the market, which means that there is a very limited amount of time left before the patent expires."

However, there are also several factors pushing startups to file for patents earlier. One of them is the ability to raise venture capital, which is supported by patents. Thus, pharmaceutical startups might find themselves stuck in a catch-22 situation; needing patents to attract financial capital but lacking the necessary capital to afford the patenting process. Another factor is that pharmaceutical startups are often based upon academic research, with founders that are eager to publish their results in academic journals as soon as possible. Because patentability requires novelty, the patent applications need to be filed before any type of publications (including academic journal publications). Early patenting also mitigates the risk of being locked out if competitors are undertaking competing R&D with a related pipeline of patent applications. Finally, patents are important to enable exits. Much of this is summarized by one of the interviewees:

⁴SEK is the abbreviation for Swedish Krona, i.e. the Swedish currency. 1 SEK = 0.12 US\$ = 0.11 € (as of early 2016).

⁵All quotes have been translated from Swedish into English by the authors.

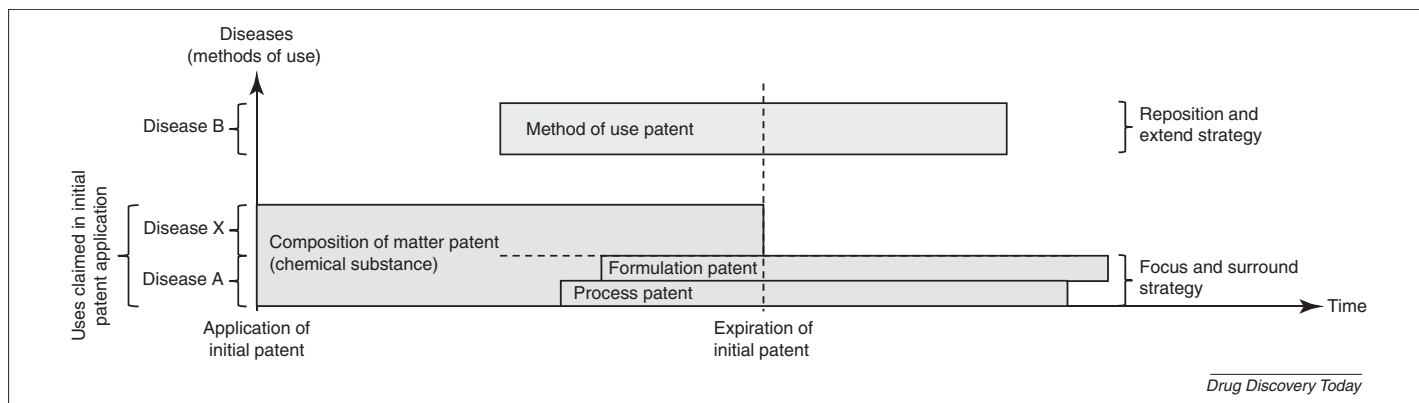


FIGURE 1

Examples of pharmaceutical patent strategies. In the focus and surround strategy an early broad patent of the chemical substance is complemented with formulation patents and process patents to strengthen and extend (in time) the patent protection related to the specific drug. In the reposition and extend strategy a new use for a previously known substance is protected by a method of use patent, thereby extending the protection time of the substance for that specific use.

“If you know that other actors are also working in the field you have to be quicker because you don’t know what they have filed or will file patents for. [...] Raising money is much easier when you have a good patent protection around you. [...] The researchers want to publish their results and then you have to make sure to file for patents before publishing. And when you get to an exit decision it is necessary to have a good patent protection. [...] Nobody is interested if you don’t have a good patent situation.”

A pharmaceutical startup (just as any pharmaceutical firm) has different types of patents to work with. These include: (i) composition of matter patents (product claims) that claim the active chemical substance; (ii) method of use patents that claim the use of the drug to treat one or multiple specific disease(s); (iii) formulation patents that claim the composition or method of application of the drug; and (iv) process patents that claim the process by which the drug is manufactured [11]. These are by and large the different types of patents that any pharmaceutical firm has to work with, albeit slightly varying across national jurisdictions. To balance the factors pushing for early and late patenting, respectively, a combination (portfolio) of these different types of patents can be used. This was exemplified by an interviewee:

“Initially we try to have a patent that is as broad as possible and that limits invent-arounds. Later on we try to

add additional patents to extend the patent protection time, possibly by patenting formulations [...] and manufacturing processes.”

The interviewee describes what could be called a ‘focus and surround strategy’ (Fig. 1). Initially, a broad patent application of the chemical substance is filed, which could cover several potential uses (diseases). Later on, the focus is narrowed down to a specific disease, and the initial patent is surrounded by a portfolio of related patents, such as formulation patents and process patents, to strengthen the protection in that specific area. Within PULS this is typically done as close to exit as possible to delay costs as well as to strengthen and extend (in time) the patent protection related to the specific drug.

Another strategy is to take a known (and probably patented) substance, reposition it for the use of a new disease (that was not claimed in the initial composition of matter patent) and protect it by for example filing for a method of use patent to extend the patent protection time. This could be called a ‘reposition and extend strategy’. For example, the basis for the DuoCort project within PULS was a formulation patent for treating Addison’s disease with a dual release (quick + slow) of the well-known substance hydrocortisone, complemented with some other patents.

As described above, the most prominent factor impacting patent management in startups is the lack of financial capital. Although delaying (some) patenting is one way to mitigate this resource constraint, another way is to limit the geographic coverage of patent protection, as illustrated by an interviewee describing one of the projects:

“Due to the financial situation [the inventors] did not have the possibility to get a broad geographical coverage of the patent protection [for the first patent].”

Every patent needs to be filed and/or validated in each country where the patentee wants protection (with related fees and other costs), and the decision of where to patent is instrumental for the future success of the startup, impacting the burn rate and the future commercial potential. The general strategy of PULS is to focus on a smaller set of countries than larger firms would probably do:

“Another part of the patent strategy is to cover the major markets, North America, EU, Japan, possibly China and South Korea.”

The logic is explained by another interviewee:

“You have to focus on the major markets which account for the majority of the commercial potential, and 80–90% of the potential sales. You have to take the risk of not patenting in some markets. The probability that someone else would develop a competing product in this country where we don’t have protection is fairly small, there are no commercial incentives for that. [...] What we look at is basically the population potential. [...] How many patients are there, and what is the price we can take. [...] So this is a difficult balance act, where to patent in relation to the costs. We chose 21 countries in total. [...] Other

projects have chosen to go broader, but that has been very costly.”

Concluding remarks

This article has pointed at the fact that pharmaceutical startups have several characteristics that require additional dimensions of consideration in patent management, compared with large firms. Patent management in pharmaceutical startups needs to be more entrepreneurial, considering additional resource constraints and a different set of strategies. The lack of financial capital could require the startup to delay patenting decisions and to limit the geographical scope of protection. A solution is to build and plan for a portfolio of patents, with an early broad patent (e.g. a composition of matter or a method of use patent) on major markets, and a pipeline of related patent applications (e.g. formulation and process patents) that can be filed close to exit to limit the burn rate, while adding as much value as possible before the exit. This type of ‘focus and surround strategy’ has been successful for several projects within PULS.

Although related to several difficulties, entrepreneurial patent management in pharmaceutical startups also carries the opportunity to improve the ‘innovativeness’ of the industry. Better patent management could enable more startups to reach further, and would decrease transaction costs in connection to interactions with large firms (such as in cases of exits) [12]. Better patent management could also incentivize the repositioning of old substances to new diseases through the use of method of use

patents or formulation patents. By focusing on patent protection and exits, the PULS network has kept a clear focus on building patent portfolios that are valuable and transferrable at the time of exit, avoiding the patent problems that are otherwise common in innovation transactions [13]. Thus, entrepreneurial patent management can play a small but important part in the process of creating a more interactive, open and innovative pharmaceutical industry.

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