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Licensing: pros and cons for biotech

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This article guides the reader through strategic considerations when facing the option to license a drug development project. It is crucial to understand these licensing events in their full complexity in order to achieve maximum value for the company and the shareholders, while minimizing risk. First, the nature of various license agreements and the needs of licensor and licensee are discussed. Second, the main strategic issues for the licensor are explained and a guideline, how to come to a decision whether to license and to what terms, is given. Third, the authors explain how to overcome different assumptions when negotiating a license contract.

Introduction

For the sake of clarity we call early stage companies, that is, companies with no products on the market, biotech companies, and their counterparts pharma.

Nature of license agreements

License deals should address the interests of both the licensee (pharma) and the licensor (biotech). The standard structure of the agreement foresees an upfront payment when signing the contract, milestone payments when certain development goals are achieved, and royalty payments once the drug is on market. The interest of biotech is to get cash as soon as possible while maintaining a share in the project if it should become a success. Pharma, on the contrary, needs attractive projects to fuel its pipeline, but wants to share the development risk with biotech. Pharma is, therefore, reluctant to pay a large sum upfront. It prefers to tie the payments to certain achievements and ultimately reward the biotech company with royalty payments. Royalties depend on economic success, and pharma does not want to spend money as long as the economic success is uncertain.

Strategic issues in licensing

In the following we will elaborate the three main questions biotech faces when out-licensing a drug development project:

1. To license at all?
2. When to license?
3. How to determine the structure of the license contract?

Since the goal of management should be to maximize the company's value we investigate the effect of different licensing alternatives on the value of the company. The reader can consult a case study, which is amended as supplementary material to this article to see the analysis of these questions at a real life example.

To license or not to license?

Large-scale phase 3 trials, regulatory affairs, large-scale manufacturing, global marketing and sales are a huge challenge for an inexperienced biotech firm. A growing biotech company has to raise capital several times until it finally generates revenue. Fund-raising is a time-consuming activity that sometimes diverts the attention from the operational business and causes delays. The market environment might not be favorable for the financing of such risky endeavors and existing investors might get excessively diluted. If the project fails at one point along the development path, most of the invested money will be lost; hence the investors take a big risk with the company's strategy to commercialize a drug on its own. Licensing the project might be a good alternative, since no further cash is required to take the project forward and part of the value can be incurred before commercialization with upfront and milestone payments. On the contrary, most investors are in biotech for the big wins [1]. If a biotech company licenses a project it gives up a lot of its upside potential. But if most shareholders are founders and undiversified individuals, the desire to secure value might be high.

The first question to ask when deciding whether to license or not is: 'Does the company need cash?' Licensing a project not only relieves the company of bearing the subsequent phase costs but also provides the company with cash

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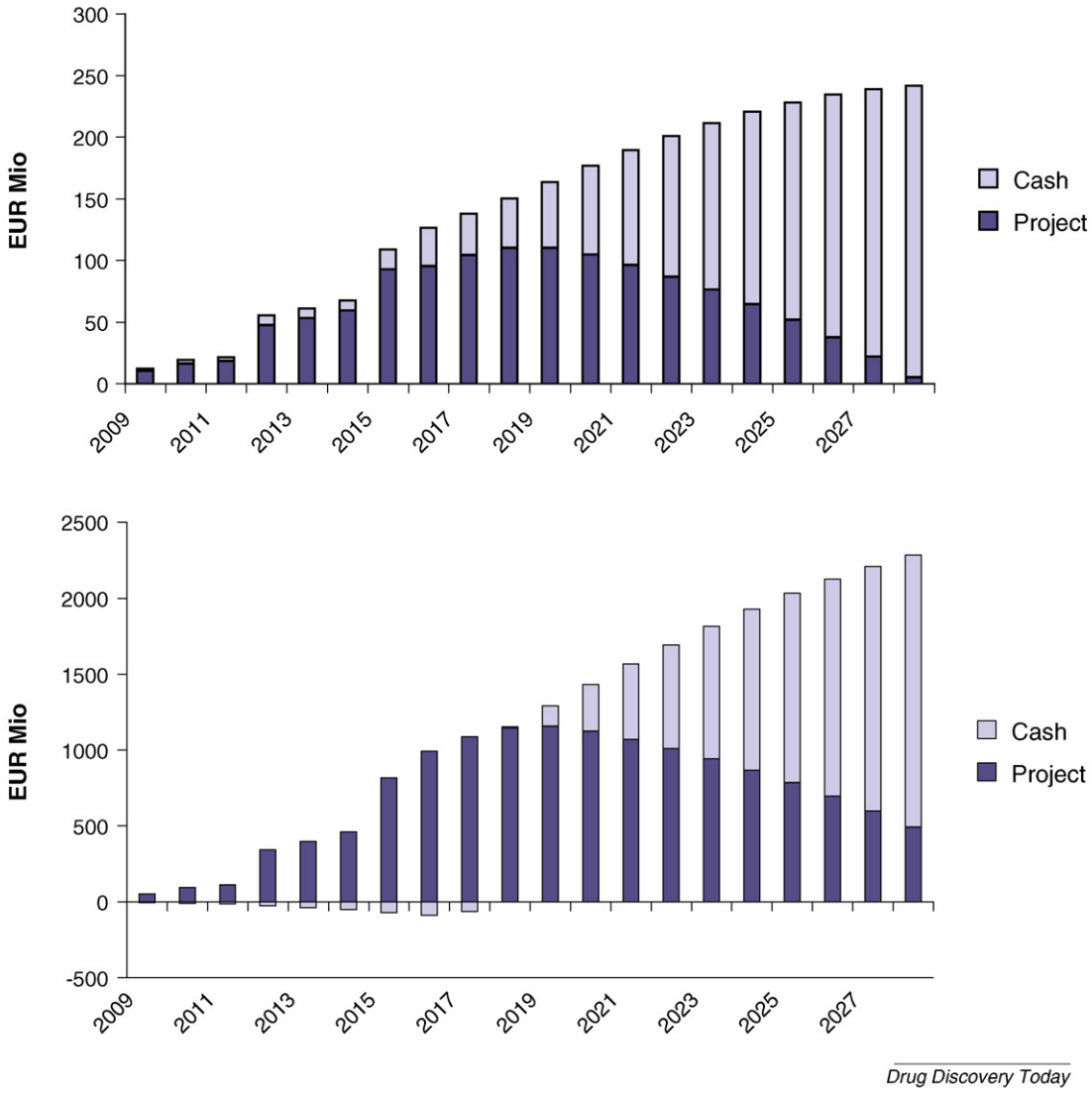

FIGURE 1

Value development of a project if self-conducted and if licensed (calculated with ri:val). The graph displays the value of a project for each year as it moves forward along the development path. While the dark pillars represent the risk adjusted net present value (value computed out of future, i.e. not yet realized cash flows), the light pillars represent the cumulative cash balance or the already realized cash flows. At the end of the project's life cycle the value has completely turned to cash.

by way of upfront and early milestone payments. This attractive liquidity concept obviously comes with a disadvantage. If the project reaches commercialization, the biotech company is now only entitled to royalty payments, instead of the sales in their entirety.

Figure 1 displays the value development of a project once if it is licensed and once if it is developed and commercialized by the biotech company to show the difference in the upside potential.

We see that in both cases the project value increases in jumps once a new phase is reached. These value jumps stem from the reduced uncertainty. In the self-conducted scenario the company has to invest into clinical trials and commercialization before potentially harvesting sales [2]. If the project is licensed, the company cashes in part of the value already with the upfront payment and then with milestones, before knowing if the project will ultimately make it to the market. As a consequence, the upside potential is much lower, as the licensor only participates in terms of royalties, which usually are much lower than operating benefits from commercialization. Figure 2 displays the different risk profile of the two strategies. When commercializing the project, then the company runs the risk of economic loss (red pillars) and consequently requires more cash, but at the same time the good scenarios are much more valuable.

The second question focuses on additional benefits in a licensing deal. Does the company get access to know-how and expertise of the partner and does it require a proof of concept that would be given by the closure of an agreement with big pharma? Biotech companies often are not used to running large-scale trials and dealing with regulatory authorities. Teaming up with an experienced industry player not only fills that gap for the project in question but also allows the biotech company to gain experience. Most companies already try to reduce this lack of experience by putting ex-pharma employees into key positions of the biotech company's management, but these managers cannot always compete with a whole department

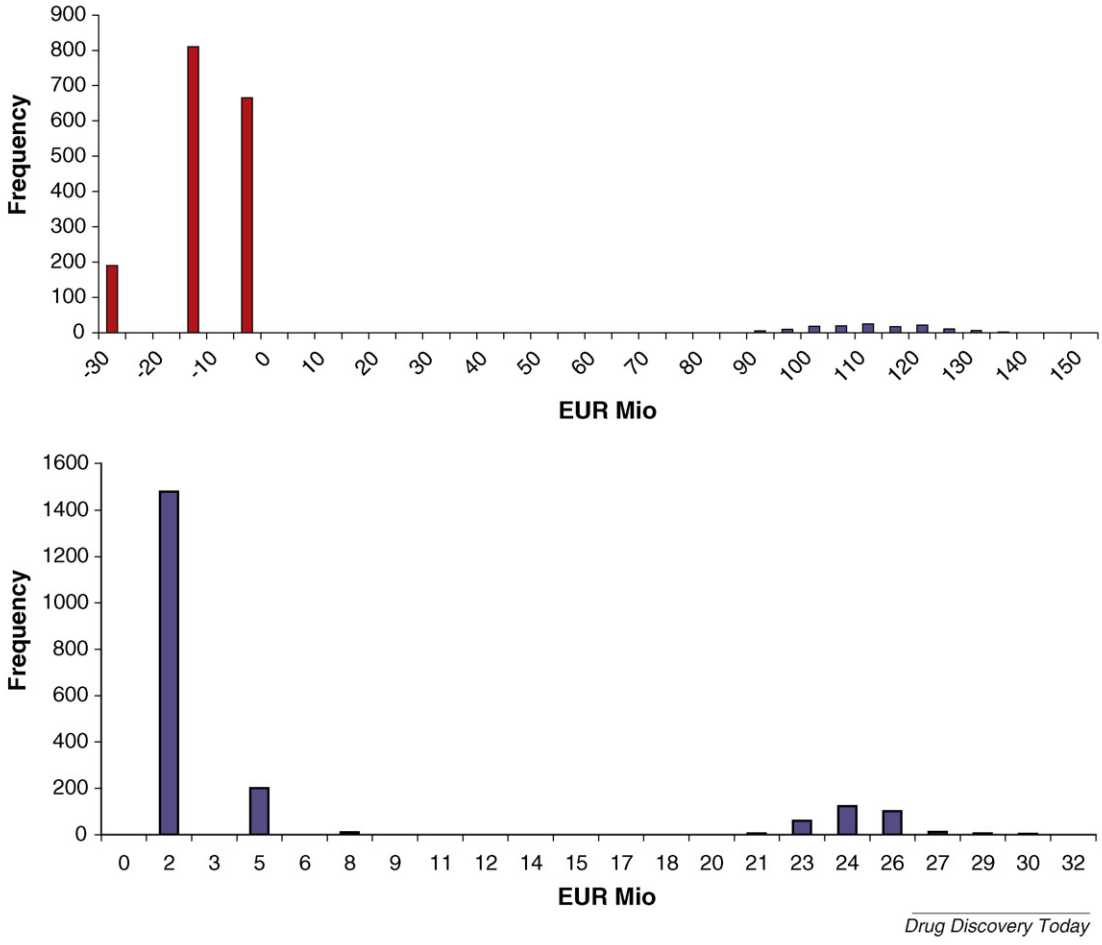

FIGURE 2

Risk profile for a project if self-conducted and if licensed (calculated with ri:val). The graph displays 2000 Monte Carlo simulations. Each column indicates the number of scenarios that have a value falling in the range covered by the column. Red indicates negative values, blue positive values. The dotted line represents the mean value. For the pharmaceutical company (upper graph) the red pillars represent the scenarios where the project fails in a clinical phase and all expenses are lost, while the positive blue scenarios stem from commercialization. Biotech (lower graph) even earns money if the project fails in development, albeit the value stemming from royalties (scenarios on the right end) is much higher.

focused on clinical trial design, regulation or marketing. Another advantage of licensing is the proof-of-concept effect. New approaches, whether in medicine or elsewhere, are always difficult to evaluate. After the investment bubble at the beginning of this millennium, new technologies were usually valued rather conservatively. If now a well-reputed industry player licenses such a new technology, this contract is perceived as if an expert affirmed the company's claim that the technology is promising. Moreover, the pharma company is even ready to spend money on this technology. This signaling effect facilitates fund-raising. After such a deal it is easier to defend a higher valuation and therefore limit the current shareholders' dilution. If the company has a full pipeline leveraging on its technology, such a lighthouse agreement might increase the company value significantly.

In order to come to a decision the biotech's management must compare the different scenarios and also factor in the outlined qualitative aspects. If licensed, then the cost of capital for the biotech company is likely to go down, because an expert pharma company addresses the main risks. A pharma company might also achieve faster and higher sales, as it can lever on its sales and distribution network. The self-conducted scenario should probably use more conservative assumptions in terms of costs and duration of the development of the project, as biotech is inexperienced in this.

The biotech company must be aware of its capabilities of raising funds and keeping its timelines and should consider the preferences of its shareholders when facing the question whether to license or not.

When to license?

Actually, the more valid question should read: Should we license now or conduct the next phase on our own? If the company decides to develop the project on its own it can then still evaluate its situation again after the phase has been completed. In order to compare the two alternatives we have to value the two scenarios. For this exercise we have to make some assumptions. First, we must estimate what license contract we could negotiate after that phase, that is, how does a hypothetical phase 2 license contract compare to the license contract for the same project in phase 1? This must be put into context with the success rate of getting to the next phase and the associated costs (for valuation and license terms please consult [3]). Second, we must account for the time of closing the license contract and, even more importantly,

for the likelihood of closing such a contract. Not every project can be licensed. Many projects in clinical development are on hold because no licensee can be found and the companies cannot or do not want to bring up the capital to move them forward. Before relying too much on the scenario that the project will be licensed after having reached proof of concept in man, a biotech company is well advised to feel the temperature to see whether the project actually is licensable.

How to determine the structure of the license contract?

If the biotech company wants to license the project it still is left with the question of how to structure the contract. Biotech companies usually are in constant need of cash to fund their other R&D activities. Therefore, they prefer large upfront and early milestone payments. This way they can delay another fund-raising round, wait for a potential jump in value of the company due to clinical news from one of their projects, and subsequently reduce the dilution of shareholders. On the contrary, the remaining value of the licensed project is significantly reduced because a large part of the value has already been locked in with the upfront and early milestone payments. The structure of the license deal is therefore closely related to the situation of the company. If the project is the backbone of the company it might be advisable only to license parts of the rights on the project and keeping still some significant upside potential. The biotech company can, for instance, retain the commercialization rights of Europe or the USA. Recent deals indicate that biotech companies increasingly negotiate co-commercialization clauses. These can contain co-promotion or exclusive promotion in some countries, or profit (and loss) sharing.

As long as the biotech company would like to maintain or even grow its R&D activities, R&D funding is an attractive option. It is usually assumed that the licensee funds all R&D in its own facilities. R&D funding provides biotech with the necessary cash to develop the project at their sites and develop new expertise. Since biotech's researchers are already familiar with the project and the technology this can be in the best interest of both parties.

An already mentioned aspect is the signaling effect of a license agreement with a pharmaceutical partner. Often the press releases just exhibit the overall sum of milestones and call it then an US$ X Mio deal, which is confusing. This number is a simple sum of all milestones that has little to nothing to do with the value of the deal. Biotech companies tend to include various indications with separate milestones into the deal, just to increase the overall sum of milestones for the press release misleading readers about the true meaning of the numbers. The inclusion of backup molecules then doubles or triples this sum, although the scenario when all milestones would be paid out, that is, all backup compounds reach market, is highly unlikely. Since it is common not to disclose royalties, some companies even add commercial milestones to the term sheet, which replace parts of the royalty payments, but add to the milestone sum. It is important to remember that a manager might not necessarily have the same interests as the shareholders of a company. A nice deal headline might be more valuable to a manager and his future career than the actual value of the deal, which might remain undisclosed. Owing to the imposed opacity of press releases – pharmaceutical companies usually do not want to disclose the deal terms in full – it is problematic for managers to communicate how good a license deal they managed to close. Often only the upfront payment, the total sum of milestones, and maybe a vague indication of the size of the royalty rate are mentioned. Investors must then try to read between the lines and judge the quality of the deal.

Conclusion

Biotech companies are confronted with the decision whether to license their projects or develop and commercialize them on their own. There is no definite answer to which model is better. For general practitioner products it might be better to look for a commercialization partner with a strong sales force. A niche product could be commercialized by even a small company. On the contrary, development and production could require a more experienced company even for a niche product. For the biotech company it is important to analyze the different options that are available. Most often it does not have to decide whether to accept a term sheet or conduct the project on its own. It can modify the term sheet such that it meets its needs, or it can decide to go on with the development and face the same analysis one phase later. A sound valuation gives the management the necessary metrics to get to a decision. Often value is not even the most important factor, but rather risk profile or possible value development over the next couple of years in order to reduce dilution of current shareholders.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.drudis.2008.11.014.

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