

The economics of licensing contracts

Richard Mason, Nicos Savva & Stefan Scholtes

Understanding why licensing works in biotech, and why deals are structured as they are, will help the entrepreneur negotiate.

What makes an outright sale of technology assets, such as drug discovery technologies or drug candidates, difficult? Why does licensing work better? What are the economic trade-offs between different licensing features such as up-front fees, annual fees, milestones and royalties, and when should one be preferred? What mitigation strategies exist to limit commercial disappointment in the future? Bioentrepreneurs who wish to build and grow a successful business need to understand the economics behind these questions.

Economists are interested in incentives. Specifically, but not exclusively, they are interested in the commercial incentive of companies to deliver a competitive return on the capital of their owners, the shareholders. At times economic incentives can be perverse, but understanding when these incentives are created by contract designs, and how their effects can be limited, should help licensors and licensees develop partnerships that are more resilient.

Why not sell new outright?

Most goods, from trainers to Picasso paintings, are sold in a direct monetary transaction. Why are such simple sales not commonplace in technology transfer contracts? There are two main reasons: uncertainty and asymmetric information.

*Richard Mason is at Advent Venture Partners LLP, 25 Buckingham Gate, London SW1E 6LD, UK. Nicos Savva is at the Centre for Financial Analysis and Policy, Judge Business School, University of Cambridge, Cambridge CB2 1AG, UK. Stefan Scholtes is at Judge Business School, University of Cambridge, Cambridge CB2 1AG, UK.
e-mail: richard.mason@adventventures.com, n.savva@jbs.cam.ac.uk or s.scholtes@jbs.cam.ac.uk*

Box 1 Description of different licensing contracts

1. Up-front fees: one-off transfers from the licensee to the licensor
2. Annual fees: fixed, preagreed annual payments from the licensee to the licensor, as long as the licensee is using the intellectual property
3. Milestone fees: upon the completion of a stage of development (such as a clinical trial) the licensor receives a lump sum preagreed payoff. The milestone payoff is often thought of as a reward for good science
4. Fixed royalty fees: upon the launch of the new product, the licensor receives a fixed percentage on the total sales. Royalty fees can be interpreted as a reward for commercial success
5. Volume-dependent royalty fees: similar to fixed royalties, except that the royalty level is an increasing function of the sales of the new product

Determining the 'right' price for an asset is difficult when there is significant uncertainty about the value that can be extracted in the future—and who would deny that this is the case for a drug candidate? There are other assets available for outright sale that have a highly uncertain return—company shares, for example. But there are two key differences between company shares and drug candidates. First, company shares are frequently traded (if stock underperforms, a buyer can sell his or her shares to the market). Damage is controlled at low-transaction costs. Second, there is ample publicly available data about listed companies, not the least of which is historic stock prices, that can be used to estimate future performance. Drug candidates score badly on these two metrics. Selling an underperforming drug is very costly, and there is no comprehensive list of historic market prices for that specific drug to allow a potential buyer to estimate the current market value. When a drug is sold, all that is known is that the drug is going to cost a lot of money before the buyer sees any return. A licensor who sells the drug outright is transferring this financial risk to the buyer, and that total transfer of risk comes at a high cost. It will significantly reduce the price that can be demanded for the drug.

Asymmetric information accounts for the second reason why outright sales are not usually observed in technology transfer contracts: the seller has more information about the drug than the buyer. This leads to what the economists call the 'lemons problem', which was first studied in the '70s by Nobel Laureate George Akerlof, who used the market for used cars as his celebrated example. A potential buyer will ask: Why does the bioentrepreneur want to sell the drug? There may be very good reasons, such as difficulty with financing the next stage of development, but one possible reason is that the drug is a 'lemon'. The potential buyer won't know. The bioentrepreneur, however, has privileged information about the product, just like the used-car seller, and may well have good reasons to suspect it to be a lemon. Knowing this, the buyer will offer a lower price to compensate for the risk of buying a carefully disguised lemon. If the drug is really good, the owner will not accept this lower price and will try to find other ways of financing it. Therefore, what's left in the market is mainly mediocre drugs—as is the situation with used cars. Again, potential buyers will account for this low-value sales pool and further lower their offers, which leads to a vicious circle.

Table 1 Examples of performance clauses

Diligence payments	Payments that are required in order to continue the license (for example, a continuation milestone payable on the third anniversary of the signing of the contract)
Performance conditions	Events that are required to happen by defined timepoints (for example, if the first clinical trial is to be commenced no later than 31 July 2010). Consequences of failing to meet a timepoint could include termination of the license or require an additional payment to be made in order to continue
Diligence tests	Tests that can be set to determine whether a licensee is diligently prosecuting the development of a technology asset (for example, the minimum project expenditure within any 12-month period can be no less than X amount, or the maximum gap without any patient dosing in clinical trials can be no greater than Y months). Consequences of failing to meet diligence tests could include termination of the license or require an additional payment to be made in order to continue

Asymmetric information about the drug value can destroy incentives to participate in a direct sale even though both parties would benefit from it. We should stress that we are not presuming that bioentrepreneurs will behave unethically by lying to potential buyers about the prospects of their drugs. The asymmetric information problem arises because the buyer cannot verify that the seller is telling the truth. In summary, if a drug candidate is sold outright, then the seller would have to accept a heavy discount to account for complete risk transfer and asymmetric information.

Licensing contracts

Licensing contracts are considerably more complex than outright sales and have features that allow the parties to spread cash transfer over the life cycle of the drug (Box 1). These features can be combined and negotiated to help the parties find a contractual sweet spot that limits the asymmetric information and implements a sensible sharing of the risks involved in the project.

Licensors and licensees often will have very different attitudes about financial risk. A pharmaceutical company with hundreds of ongoing drug projects can easily absorb the failure of several of them provided there is a sporting chance of success for any one project. An inventor, however, may only have one egg in the basket. Therefore, it is generally desirable that the larger, less risk-averse partner takes on more of the risk. A licensing contract that includes milestone and royalty payments can be fine-tuned to achieve such risk sharing without requiring the licensor to contribute to the ongoing costs of the project. The licensor can defer receiving payment for his technology until the project either has successfully completed some technical development hurdles (milestone payments) or is actually generating revenue for the acquirer (royalty payments). This is equivalent to selling a product and allowing the new buyer to test it and pay a price according to how the new product's performance evolves.

Licensing contracts have a second interesting feature to deal with the asymmetric information problem: they allow the licensor to signal the quality of their invention by shifting payments to later stages of the development process. If the licensor knows that his project is good and has a higher chance of succeeding than the licensee is willing to accept, then he can ask for higher late-stage milestones and royalties as opposed to up-front fees and early-stage milestones.

Licensing contracts work for biotechnology projects for two reasons. First, the inventor is protected by rigorous intellectual property laws that forbid anyone from using the technology without properly attributing (and paying) for it. Second, the quality of the product, and therefore its value to the acquirer after the completion of technical development, is observable to both parties and is verifiable by a court if necessary. This way payments can be contingent upon properly defined technical success. Similarly, sales of the drug will be observable and verifiable because the licensee has to declare its income for tax purposes, and thus royalties can be implemented.

Although the flexibility of licensing contracts offers advantages over direct sales, they are not without pitfalls. Licensing contracts are long-term dynamic agreements, which means that during development, information about the project and its commercial value is revealed, changing the circumstances for the licensee. The contract is then interpreted in light of the new information, sometimes leading to perverse incentives.

Project-level effects

During its long and risky development process, the project will undergo a reevaluation by the owner whenever a major capital commitment is required. Such continuation decisions look to the future and discard sunk costs. Roughly speaking, the project will be stopped if the licensee's expected future revenues, accounting for the risk of failure, do not cover expected future costs. The licensee will have to pay all

future costs, but its revenues are reduced by the royalty payments to the licensor. It is therefore possible that a project that is economically viable without royalty payments will fall below the licensee's continuation threshold once the royalties are added. In this case, the contract makes a profitable project unprofitable for its owner (the licensee). This is bad news for the licensor too, who will not receive any royalties if the licensee stops the project. This problem becomes more pronounced when both the royalty rate and the uncertainty about the project's revenues are high. Therefore, overselling a drug will increase the chance of termination.

It is not only during development that incentives affect the fate of a drug. The ongoing court battle between Biota (Melbourne, Australia) and GlaxoSmithKline (GSK; London) about the marketing of the Relenza (zanamivir for inhalation) flu drug illustrates this. In 1999 the drug was approved in the United States and rapidly gained a market share of 40%. But when Tamiflu (oseltamavir phosphate) entered the market, Relenza's share dropped sharply, which had obvious adverse effects on Biota's 7% royalty revenue. Biota is 'seeking damages for GSK's failure to use their best endeavors to develop and market Relenza'¹. From an economics perspective, royalties can limit the owner's incentive for aggressive downstream investment.

There are various mitigation strategies against this problem. A variable royalty agreement, with escalating royalties as sales increase, improves the value share for the licensee if the sales projection deteriorates. A penalty payment, payable to the licensor upon termination for commercial reasons, will increase the licensee's cost of termination and render that option less likely.

Alternatively, a take-back clause can be included in the contract. Such clauses give the licensor the right to reclaim the asset under certain circumstances. This should ideally include the transfer of all regulatory filings, data and intellectual property related to the project, enabling the licensor to 'step into the shoes' of the licensee. However, when such take-back clauses are eventually activated, value can already be lost because of delays, and finding a new partner can be difficult as the licensor will have to explain why the previous partner is no longer interested. Nevertheless, the option to reclaim the asset preserves some value for the licensor.

Renegotiation would seem to be the natural reaction when royalty payments trigger termination. However, renegotiation is difficult, costly and time consuming. The licensee, having developed the drug for some time, now has more information about it than the licensor. The issues of asymmetric information and

Table 2 The performance of different licensing contracts

Contract feature	Does the contract share the risks of drug development?	Does the contract give a quality signal?	Project-level effects: does the contract increase the chance that the pharmaceutical company will lose financial interest in the future?	If the pharmaceutical company loses interest in the project, does the contract make it more likely to return the drug?
Up-front fees	No	Yes; bad signal	No	No
Annual fees	No	Yes; bad signal	Yes	Yes
Technical success milestones	Shares technical risk but not market risk	Yes; high early-stage milestones send a bad signal, while high late-stage milestones send a good signal	Yes	No
Fixed royalties	Shares technical and market risk	Yes; good signal	Yes	No
Variable royalties	Shares technical and market risk	Yes; good signal	Yes, but less so than fixed royalties	No

the lemon problem arise again, this time with the licensor being the less informed party. Carefully structured contracts (those with take-back clauses), can significantly strengthen the bargaining position of the licensor in such renegotiations.

An example of a successful renegotiation is the 2002 agreement between ImClone Systems (New York) and Bristol-Myers Squibb (BMS; New York) over the cancer drug Erbitux (cetuximab). Their relationship had deteriorated after the Food and Drug Administration rejected approval of the drug, which was developed by ImClone. Although ImClone suggested that it did not have to renegotiate its partnering deal, it was keen to maintain BMS's involvement in the development and in the end agreed to substantially revised terms, in favor of BMS.

But renegotiation attempts are not always successful, and the story around CDP870 is a prime example. The rheumatoid arthritis and Crohn's disease drug was developed by Celltech (Slough, UK) and licensed to Pharmacia (subsequently acquired by Pfizer) in a generous licensing deal, involving payments of up to \$165 million and a 40% share in profits. In 2003, while the drug was in phase 2 trials, doubts were raised about whether it was sufficiently differentiated from competing drug candidates destined to reach the market first. Pfizer (New York) thereupon attempted to renegotiate the deal. Celltech, now part of UCB (Brussels) refused to renegotiate, invoked the take-back clause, completed development and has recently launched CDP870 on the market as Cimzia (certolizumab pegol).

Portfolio-level effects

When the licensee is making its continuation decisions, it will not check the economics of the licensor's drug in isolation, but rather it will determine the value this drug adds to the licensee's drug portfolio. There may well be other drug candidates in the portfolio, at different stages of development, that are now estimated to be more profitable or that even target the same market

and have more promising performances than the drug candidate in question. The drug might be economically viable by itself, but not as part of the portfolio. In 2001 Oxigene (Waltham, Massachusetts) experienced that problem with its drug CA4P, licensed to BMS, when BMS in-licensed ImClone's Erbitux mentioned above. Richard Chin, Oxigene's CEO and president, commented in a *Nature Biotechnology* article: "It was clear that Bristol-Myers had reprioritized their portfolio. The effort they were putting into the drug was starting to be less than what we thought was appropriate. It's not great to have a partner if they are not moving the drug along as quickly as you might want. In fact, it's better to get the drug back, rather than have it languish"².

A termination decision is not necessarily clear-cut. It may well be in the licensee's economic interest to slow down the development and keep the drug alive as an 'active backup'—an insurance policy if other drugs don't develop as expected. (Indeed, one of the authors has experienced this firsthand.) Selling the rights to a competitor might not be in the licensee's interest if it could threaten the existing or projected future income stream. Because the licensor will find it difficult to directly observe if the project is actively pursued and even more difficult to prove in court that it is not, any take-back clauses might be difficult and expensive to execute. Even if the drug is eventually handed back, the delay and possible reputation taint may destroy its value.

An annual fee is a possible defense against portfolio effects because it makes slowing down development expensive. Substantive annual fees, however, would erode the aforementioned advantage of licensing contracts to allow for cheap information acquisition, especially if the project has a high chance of late-stage failure.

The main mitigation strategy against portfolio effects is due diligence, including a review of the fit of the new drug with the licensee's existing portfolio and competitive position,

backed up by conversations with the licensee's scientists who are likely to work on the drug. The contract itself could also contain specific performance conditions. Failure to meet these conditions could trigger penalty payments or even force the licensee to return the drug (Table 1).

Summary

A licensing contract, with its flexible mix of up-front payments, annual fees, milestones and royalties, possible termination fees and so forth, has economic advantages over outright sales because it permits risk sharing and provides an effective way to reveal more information about the drug. However, licensing has pitfalls too, which must be understood by the licensor. High milestone and royalty payments can render a commercially viable drug uneconomical for the owner. Changes in the licensee's portfolio or prioritization strategy can lead to a commercially viable drug falling off the radar screen, relative to the licensee's alternative investment opportunities, which can lead to a slower development, less downstream effort or even termination. However, different clauses in licensing contracts can help mitigate these issues (Table 2).

Although designing robust contracts is important, there is no foolproof contract. Contract structures can never be a substitute for meticulous due diligence and effective alliance management.

Finally, as licensing passes all of the costs and most of the risks of development to the licensee, the licensee will typically demand a large share of the value. If the licensor wants a larger share of the upside potential of the project, then different contract forms that permit more risk-taking in a controlled manner may be more appropriate than standard licensing deals.

1. Cook, P. Progress on GSK litigation – letter to shareholders. *Biota Holdings Limited* <[http://www.biota.com.au/uploaded/154/1021188_02lettertosshareholders.pdf](http://www.biota.com.au/uploaded/154/1021188_02lettertoshareholders.pdf)> (2006).
2. Hugget, B. *Nat. Biotechnol.* **25**, 841–843 (2007).