When To Deal: Implications Of A Model For Optimal Timing

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Introduction

When licensing a pharmaceutical technology, there is no clear consensus on the best time to do the deal. With varying stakeholder interests and numerous factors to consider, the task of finding the optimal time to out-license a pharmaceutical technology is far from straightforward.

To gather opinions on what stage of development is perceived as best for completing a licensing transaction, Campbell Alliance conducted a deal-making intentions survey of nearly one hundred licensing professionals in the pharmaceutical industry. Study results demonstrated variations between what in- and out-licensors stated was the ideal timing for a deal and when the historical record demonstrated the deals were actually getting done.

To facilitate decision making on out-licensing, most organizations start with quantitative financial assessments; however, strict quantitative analysis is frequently insufficient to make a fully informed decision on whether and when to out-license. This article provides a quantitative model that objectively investigates optimal timing for out-licensing and further discusses qualitative factors that could shift the decision-making process away from one strictly driven by the numbers. The compelling findings and implications from the model are presented.

Disparate Views on Best Time to License

During development to earn market approval, a drug must be tested in three phases of clinical trials. If the drug meets predetermined clinical endpoints in the studies, it can gain permission from the FDA to move forward into the next phase. With very high attrition rates during this development process, meeting clinical trial hurdles and moving into the next phase lowers the risk that the drug will never make it to market, and thereby increases its value in a licensing transaction.

A deal-making intentions survey of the pharmaceutical industry was conducted to seek opinions on what stage of development was perceived as best for completing a licensing transaction. The study found that over 70 percent of in-licensors agreed that the preferred time to license a technology is within phase II (Figure 1). Interestingly, there was far less consensus among out-licensors. Although “during phase II” was also the most cited response, this was chosen by less than half of the respondents, while over one-third selected “during phase I” as the best time to complete a deal. It is perhaps not surprising that a greater number of out-licensors suggested they would like to complete the deal at an earlier stage, as out-licensors typically want to deal earlier than in-licensors. Also, the recent financial environment—a non-liquid financial market and low cash on hand—further rationalize the differing results among respondents.

A study of historical data for trends in pharmaceutical licensing transactions from the past several
years demonstrates a shift to licensing transactions occurring in later stages of development (Figure 2). The data suggest that in-licensors are increasingly becoming more selective in the choice of products they will license. More specifically, in-licensors are looking for assets that have passed proof-of-concept and are somewhat de-risked.

Clearly, the disparities between historical transaction timing and the results of the survey indicate that a variety of factors can affect when a deal actually gets done. This article sets out to objectively quantify the best time to out-license a compound. As optimal licensing timing relies on more than quantitative valuation analyses, subjective considerations that support making an informed decision are also discussed.

Quantitative Approach to Assessing When to License a Compound

To objectively assess the optimal timing to conduct a deal, a quantitative model using a decision tree analysis was conducted looking at licensing valuations for assets in different stages of development. Comparing “intrinsic value” of the asset against licensing valuations for deals conducted in phase II or phase III determines if and when to out-license a compound. As optimal licensing timing relies on more than quantitative valuation analyses, subjective considerations that support making an informed decision are also discussed.

Intrinsic Value

Frequently, the first step of a financial analysis is the estimation of the underlying intrinsic value of an asset based upon the key revenue and cost drivers. When assessing a specific asset, revenue drivers will include the market potential, competitive environment, pricing, and adoption rate, while cost drivers include clinical development, cost of goods sold, promotional needs, and size of sales force. For the model developed in this article, revenue and cost drivers have been estimated to be that of typical assets based upon previous work at Campbell Alliance.

Cash flows for an asset are dependent upon the estimates for revenue and cost drivers. The analysis described here focuses on hypothetical values of the above for an “acceptable product” with $350 million in peak revenue and $100 million in annual costs, thereby assuming $250 million in peak cash flow for the fictional product. As a comparator, each of the top 200 prescription medications had annual worldwide sales greater than $480 million in 2008 (Med Ad News, July 2009).

For the calculations, a four-year uptake curve to peak sales was assumed along with a further twelve years of patent protection. Using a 15 percent cost of capital, the present value of the cash stream was estimated at $634 million. The cumulative costs for development until registration is estimated at $120 million. At a 90 percent success rate of application approval and bringing the product to market, the net asset value is calculated to be $451 million if the company opts to self-commercialize (Figure 3a).

Licensing Values

Following the calculation of the intrinsic value, the value from a licensing transaction of the asset is estimated. Finding likely licensing terms is the next challenge. To accomplish this, historical data of previous deals are an effective means to obtain probable license terms. For the model, data from the Licensing Executives Society (LES) royalty rates survey and a third-party database of oncology products were utilized to estimate deal terms (Table 1). These sources helped define values of up-front payments, development milestones, sales milestones, and royalty rates. For the purposes of the decision tree analysis, data from both sources were leveraged to estimate deal terms for the product used in the model.

As with intrinsic value, likely licensing terms are variable and are based on assumptions surrounding the outlook for product performance, expectations of deal terms, remaining time and costs to develop, and assessments of the risk of development success. Using the likely terms in a decision tree analysis that integrates probabilities of success for phase II and phase III programs, the value of the licensing deal can be estimated (Figure 3b). With these conditions, the decision tree analysis calculated a phase II deal to be worth $52 million, while a phase III would be worth $118 million.
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Figure 3a. Product Intrinsic Value

Financial Analysis of If and When to Out-License

Comparing product intrinsic value with the licensing values according to development stage should provide insight into if and when the best time would be to license a drug. Clearly, the analysis indicates that licensing values fall short of intrinsic value and a potential out-licensor could generate greater revenue by choosing to self-commercialize the asset rather than out-license. The decision tree analysis revealed a significant inflection point when the out-licensor develops the product to phase III (value rise from $52 million to $118 million), suggesting financial benefits to deferring a license agreement. Although these findings were derived from quantitative measures, waiting to license may not always be a viable option for companies as several pragmatic factors can influence if and when a deal should be done.

Further Considerations for License Timing

Through a systematic and rational approach, quantitative measures of asset value and likely licensing

Table 1. Comparison Of Deal Terms Between LES Survey And Third-Party Database

Source: LES Royalty Rate Survey and Windhover Strategic Transactions Database. Available at www.windhover.com.
Note: Numbers used for licensing valuation were from shaded rows. LES survey divided timing into PC, pre-POC, and post-POC. Royalty rates used were 8% (PC), 10% (PI), 18% (PII), and 30% (PIII).
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terms can provide numerical values that can help direct a decision on if and when to out-license. Unfortunately, hard numbers are frequently insufficient for making an informed decision, and executives must consider other factors, including the current licensing environment as well as internal factors to the company.

External Factors: Licensing Environment

The licensing climate surrounding the pharmaceutical industry can impact the timing of when to out-license. Some therapeutic areas are considered highly attractive and generate more deals in earlier stages of development. Economic conditions can also affect deal timing. The recent economic downturn led to a restricted financial market, limiting capital and disproportionately impacting small pharmaceutical and biotechnology companies. Many of the smaller pharmaceutical and biotechnology companies had less than a year of cash (Figure 4) and were trading at a value lower than book value. These cash-strapped companies have been forced to consider earlier out-licensing to generate much needed capital.

Although the existence of undervalued companies might lead to an assumption that investors and larger companies would be licensing more technologies at bargain prices, analysis demonstrated that there was a substantial drop in large phase II deals executed in the second half of 2008 (Figure 5). This drop is partially explained by the fact that several large companies at that time had little capacity to take on more phase II or phase III assets, especially since in-licensing assets imply that a company may have to de-prioritize other products within its portfolio. As such, one might conclude that uncertain economic and corporate

![Figure 3b. Licensing Valuations For An Asset In Phase II Or Phase III](image)

Source: Campbell Alliance analysis

![Figure 4. Cash On Hand Of Emerging Companies](image)

Source: Campbell Alliance analysis
conditions caused the large in-licensing companies to shy away from good deals.

**Internal Company Factors**

In addition to external influences, several intrinsic factors also impact optimal timing of out-licensing. Factors related to the company’s finances and objectives, risk tolerance, and stage of evolution can all influence when and if to license.

Company management and the board have many considerations to take into account when deciding whether to license. Clearly, company finances are one of the most basic factors to acknowledge. If the organization does not have and cannot raise the capital needed to fund further studies, considerations of further development and self-commercialization options are moot. A typical phase III trial can require an investment of anywhere from $20 million to $100 million (or more); as of the end of 2009, less than 20 percent of publicly traded biotech firms had more than $50 million in cash. Alternatively, the company may not have experience or expertise in product commercialization, and it may not be part of the corporate objectives, thereby limiting the viable options available.

A company’s risk tolerance can also factor into the decision of when to license. According to industry estimates (used in the decision tree analysis), assets in phase II have a ~60 percent chance of never reaching the market, while out-licensing can finance a large share of previous development costs even if the product fails in trials. The risk of failure at phase III is reduced to ~35 percent, but the cost of failure is far greater since the company is paying the bill itself for the larger studies. Adjusting for risk tolerance suggests that the decision to out-license would optimally occur prior to initiation of phase III, in order to avert the risks associated with high costs.

The evolutionary stage of the company can further determine views on when to license. Factors that define the corporate evolutionary stage include financial structure, number of products in development, and anticipated returns on its products (Table 2). The very factors that determine evolutionary stage also affect the objectives of the organization, the finances, and the level of risk tolerance, which subsequently impact the licensing outlook.

**Optimal Timing to Out-License and Implications**

When a company determines that it does not wish to self-commercialize the product, the analysis can further focus on finding the optimal time to out-license. Given that there are two parties to the deal, the question of “when is the best time to do the deal?” will depend upon which party is asking the question. Optimal timing for out-licensing can be determined based on the identification of an appropriate inflection point (i.e., identification of the point in development when further development and risk will result in an insufficient ROI). The decision tree analysis of the product with peak cash flow of $250 million demonstrated a two-fold increase in valuation ($52 million to $118 million) when the

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**Table 2. Company Factors That Influence Deal Timing**

<table>
<thead>
<tr>
<th>Type of Company</th>
<th>Structure</th>
<th># Products/Revenue</th>
<th>Anticipated Returns</th>
<th>Level of Risk Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-Molecule Shop</td>
<td>Private &quot;Single VC&quot; funded</td>
<td>1-2 products, no revenues</td>
<td>High</td>
<td>Moderate to High (willingness to risk proportionate to level of funding)</td>
</tr>
<tr>
<td>Development Shop</td>
<td>Private, funded by several large VCs</td>
<td>3-6 products, no revenues</td>
<td>Moderate to High</td>
<td>Moderate to High (willingness to risk proportionate to level of funding)</td>
</tr>
<tr>
<td>Specialty Pharma</td>
<td>Public</td>
<td>Several in-line and pipeline products</td>
<td>Moderate</td>
<td>Moderate to High</td>
</tr>
<tr>
<td>Large Pharma</td>
<td>Public</td>
<td>Several in-line and pipeline products</td>
<td>Low to Moderate</td>
<td>High</td>
</tr>
</tbody>
</table>

Source: Campbell Alliance analysis
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product achieved phase II success, thereby showing a greater than 100 percent return from the investment in phase III trials.

Calculating licensing valuations for hypothetical assets with peak cash-flows of either $100 million or $500 million can assess whether this return might hold true for other compounds. Interestingly, the model demonstrates that the asset with peak cash-flows of $100 million does not increase in licensing value above the cost of development when moved into phase III, and therefore exhibits an ROI of zero (Figure 6). Conversely, the asset with the peak cash-flows of $500 million has an enhanced valuation in phase III with an ROI of over 200 percent.

The results suggest that the out-licensor should develop assets with predicted peak cash-flows greater than $100M beyond phase II to maximize future returns. For products with peak cash-flow expectations of $100 million or below, the ROI is too low to justify the investment for a small company. For such products, a company will either need to consider niche strategies (with a smaller sales force and more defined target population) that can lead to positive returns or shelf the product altogether. It should be further noted that the lower intrinsic value does not mean that all is lost for the asset, as it is possible that the out-licensing company could not realize the same self-commercialization value for a product as could another organization. A company with other marketed products could utilize potential synergies in manufacturing, distribution, and commercialization to boost revenue and profitability of a licensed product. As such, the product retains a higher intrinsic value to that company.

This analysis demonstrates that the optimal timing for out-licensing is dependent on the potential value of the asset and implies a need for a comprehensive commercial assessment prior to discussion on optimal timing of out-licensing.

**Conclusion**

Optimal timing for when to license a compound is clearly multi-factorial, and there is no single formula that provides a straightforward solution for all situations. The deal-making intentions survey conducted found that 80 percent of out-licensors prefer deals to take place in phase I or phase III; however, the analysis conducted in this article demonstrated higher valuations for products in later stages of development, providing the argument for smaller companies to develop their technologies as far as they can afford. The survey also found that in-licensors overwhelmingly prefer deals to take place later than an out-licensor would typically like.

The valuation model in this article does not take into consideration the internal company conditions and external factors that can influence if and when the deals actually take place. Clearly, the economic downturn significantly impacted when recent deals were getting done. Approximately 40 percent of small biotechnology organizations retained less than one year’s worth of cash on hand, resulting in a need to out-license early. Although an increase in earlier stage deals might be expected, this did not materialize. Large pharmaceutical companies have been filling their phase II pipelines organically and through acquisitions (Campbell Alliance analysis), potentially leaving them reluctant to license compounds due to resource constraints. At the same time, venture capital funding went relatively dry as ROIs trended downward, thereby restricting options for the small pharmaceutical company and further slowing progress in the development of compounds.

The recent economic conditions greatly influenced the licensing landscape and hampered new investments; however, the pharmaceutical industry needs to maintain a promising pipeline to preserve and increase top-line revenues. Even as the financial markets improve, it is expected that in-licensors will be increasingly selective in the products that they acquire. Small drug companies need to take this cue and focus development efforts on products that could fit targeted unmet medical needs—rather than focusing on the science behind their innovations—and should be increasingly selective with compounds they choose to develop.

Large pharmaceutical companies are increasingly playing the role of venture capitalists through their external portfolio arms and with the increasing share of deals that
are option-based. Large manufacturers have shifted some of their focus on academic collaborations for pre-clinical innovation, but are increasingly looking for assets that are post proof-of-concept, leaving a large chasm of unpartnered products with small biotech firms. Interestingly, the ever-increasing hurdle rates used by big pharma for in-licensing assets are generally higher than those employed for internal assets.

The plethora of unpartnered assets also suggests that venture capital firms have been doing an inadequate job of due diligence prior to investing. To stay within the game, venture capital firms need to step up efforts by conducting more robust due diligence and possibly adjusting to a longer horizon for exits. Typical venture capital firms are looking for a five to seven year exit horizon before moving on to the next fund. Keeping in mind that the ROI model demonstrated that longer time horizons could substantially increase the exit value, the shorter windows may be limiting the scale of the venture capital exits.

The use of consistent due diligence and hurdle rates for internal and external R&D opportunities by large pharmaceutical manufacturers; assets of portfolio companies by VC firms; and portfolios by small pharmaceutical firms will lead to a more efficient licensing market. The ROI analysis demonstrates that larger companies should be receptive to in-license assets across all stages of development, especially as they increasingly rely on an externalization model to continue to develop products. Acting on the potential bargains of in-licensing early-staged assets will help to invigorate the slowed deal trend and keep pharmaceutical innovation moving forward.