Regression Analysis of Oncology Drug Licensing Deal Values

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Executive Summary

This work is an attempt to explain wide variations in drug licensing deal value by using regression modeling to describe and predict the relationship between oncology drug deal characteristics and their licensing deal values. Although the reasons for large variances in value between deals may not be immediately apparent, it was hypothesized that objective independent variables, such as a molecule's phase, its target market size and the size of the acquiring/licensor company could explain a significant portion of variation in cancer drug values. This model, although not predictive when used independently, could be used to supplement other discounted cash flow and market based techniques to help assess the worth of incipient oncology therapies.

Using regression analysis to study drug licensing deals is not novel: a study was published by Loeffler et al in 2002 that attempted to assess the impact of multiple variables on deal value in a wide range of pharmaceutical indications. The independent variables in Loeffler's work could explain less than 50% of differences in deal values. It was expected that refining the model could lead to improved regression R squared coefficient and, potentially, be a useful tool for managers. This current work is based on the 2002 Loeffler paper, but differs significantly by:

- Focusing on just oncology licensing deals instead of deals covering many indications,
- Incorporating a measure of the assets of the larger licensee company,
- Accounting for the licensing experience of the smaller licensor company,
- Factoring in inflation and the years the deals were signed; and
- Assessing the impact of primary indication market size.

The goal of the thesis was to advance the art of estimating the value of drug licensing deals by assessing the impact of the aforementioned factors.

Methodology

This work evaluated 101 oncology partnerships signed between 1996 and 2005. Data was gathered from ReCap.com and press releases related to the individual deals. Deal value was defined as all potential licensing payments, as reported by ReCap[1]. Of the 101 molecules, 50 were indicated for a specific cancer type therefore it was possible to associate potential market size and market growth rate data with these 50 deals. Market size and growth rate were derived from Frost and Sullivan reports.

Regression analysis was conducted on the single independent variables and combinations of the variables using R 2.2.1. Two primary regression models were done: one with all 101 deals and one with the sub-set of deals with a defined oncology indication. The following hypotheses were made regarding independent variables:

[1] ReCap.com is used by many business development professionals; this source was used because the author believed it was the most complete database available.

- Phase of molecule-it was expected that later stage molecules would be more valuable,
- Assets of the licensee-it was expected that larger companies would pay more, all other factors held equal,
- Identity of the licensee (pharmaceutical company vs. biotech, as defined by ReCap)-it was hypothesized that pharmaceutical companies would pay more,
- Licensing experience of the licensor/smaller company-it was expected that licensors with few previous deals would receive less compensation,
- State of the economy (as measured by previous years' GDP and NASDAQ value)-it was hypothesized that licensing deals signed following periods of relatively brisk economic growth would be more valuable; and
- Year of the deal-all deal values were inflation adjusted, however, it was still hypothesized that partnerships later in the dataset would be more valuable due to increased licensing competition.

Results

The following table shows descriptive statistics for the two data sets.

Data Set	# of Deals	Mean	Std. Dev	Median	Range
All Cancer Deals	101	$102M	$121M	$56M	$1-541M
Pre-Defined Indication	50	$86M	$107M	$45M	$1-515M

In the regression analysis of all 101 deals, the aforementioned variables were able to explain 56.76% of variation in deal value (adjusted R-squared=52.98%). Among the 50 deals with a pre-defined indication, the independent variables explained 64.24% of variation (adjusted R-squared=55.07%). The significant predictors of value were assets of the licensee (p=5.3 e-14 when taken alone, p=9.18 e-10 in multivariate analysis) experience of the licensor (p=.004347 in univariate analysis, .06652 in multivariate analysis) molecule phase (p=.0428 taken alone, p=.00306 in multivariate analysis) and year of the deal (p=4.03 e-5 in univariate analysis, p=.00513 in multivariate analysis) were all significant positive predictors of value at the 5% level.

The following table shows the impact of independent variables among all analyzed deals.

Variable	Beta	P-Value
>2 Previous Licensor Deals	$33.91M	.06652
Prev. Years' Assets of Licensee	$4.29M per $B in Assets	9.18 e-10*
Licensee is Pharmaceutical	-$5.41M	.79727
Molecule is Biologic	$9.84M	.60475
Molecule is in Stage 2	$4.98M	.79624
Molecule is in Stage 3	$74.16M	.00306*
License is Global	$57.33M	.14234
Year	$10.28M	.00513*

The following table shows the influence of independent variables among oncology deals with a pre-defined cancer indication.

Variable	Beta	P-Value
>2 Previous Licensor Deals	$44.92M	.0483*
Prev. Years' Assets of Licensee	$3.54M per $B in Assets	2.12e-06*
Licensee is Pharmaceutical	-$28.26M	.2385
Molecule is Biologic	$23.34M	.1469
Molecule is in Stage 2	-$2.24M	.9392
Molecule is in Stage 3	$83.93M	.0162*
License is Global	$46.26M	.2386
Year of Deal	$9.52M	.0343*
Mkt. Size of Indication	$13.45M per $B in Mkt Size	.0637
Proj. Growth Rate	-$1.46M per % point in growth rate	.4688

*significant at the .05 level.

Conclusions

This work was significantly limited by the nature of available information: data from ReCap included all up-front and potential milestone payments. Deal value, when tallied this way may be representative of real value, but is inherently flawed since most of the calculated deal value may never be paid. Inclusion of future payments may have also inflated the value of early stage deals, since the study methodology treated them as if they had already reached future milestones. This bias toward early stage molecules should reduce the impact of molecule phase on the regression model.

Equally importantly, many subjective variables such as company strategy and molecule safety and efficacy are key to licensing deal values; none of these were included in the analysis. A study of key factors to licensing managers cited strategic concerns as important inputs into deal value (Loeffler et al 2002).

The current data explains, at best, only 64.24% of changes in deal value. It is hypothesized, based on inherent weaknesses in this work and conversations with corporate licensing managers, that the remaining variation could be accounted for by calculating real, probability-adjusted deal value, assessing existing drug competition in specific therapeutic areas, and somehow quantifying strategic concerns that weigh on licensing decisions. The mediocre R-squared in this work, especially given that the most significant drivers of deal value will be unaffected by business development manager actions, gives the model limited value as a decision making tool. Unfortunately, managers cannot control their companies' past licensing experience or the FDA phase of their drug candidate, although they may choose to target larger company partners to reap more value.

Ideally, more follow-up study would be done, first focused on collecting accurate information regarding the magnitude and timing of the components of total deal value. These future payments could be probability adjusted and to present value. Also, gathering information on existing competition in a given therapeutic area may make market size and growth rate more significant variables, as most individuals interviewed in association with this thesis suggested they would be. Once completed, an optimized

regression model that estimates 80-90% of deal value, combined with other valuation techniques such as risk-adjusted NPV could be a valuable for pharmaceutical managers who want to accurately price new licenses and for small company decision makers who want to earn optimal value for their compounds. Additionally, such a model could lead to understanding regarding the real drivers of drug candidate value, which could influence decision-making earlier in the planning process for all emergent pharmaceuticals.

Brief History of Licensing

The history of licensing is closely related to the history of patents, which can be traced thousands of years. A version of intellectual property rights was practiced by the Phoenicians; the first recognized patents were granted in the Republic of Venice in 1474.

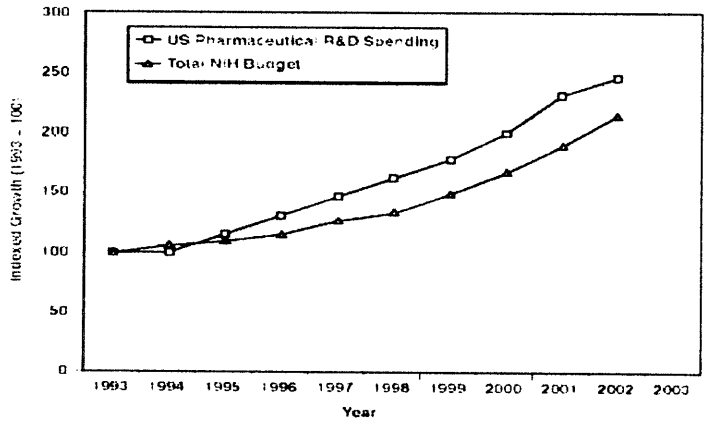
The pharmaceutical industry was the first to make systematic use of licensing in Western Europe and the United States: manufacturing licensing agreements allowed for the quick dissemination of penicillin and bacitracin during World War II. In the 1970s, pharmaceutical companies began buying the rights to screen potential compounds from other industries. Chemical companies were the primary sources of compounds due to their large libraries of new chemical entities (LESI 2001). Additionally, pharmaceutical companies in-licensed products in territories where they had existing sales forces and out-licensed drugs to other pharmaceutical companies to sell in other territories. In recent decades, licensing has taken on more importance in pharmaceuticals and emerged as a strategy in other industries.

Intellectual property author Robert Goldscheider (Goldscheider 2002) attributes the rise in the use of licensing agreements to four factors:

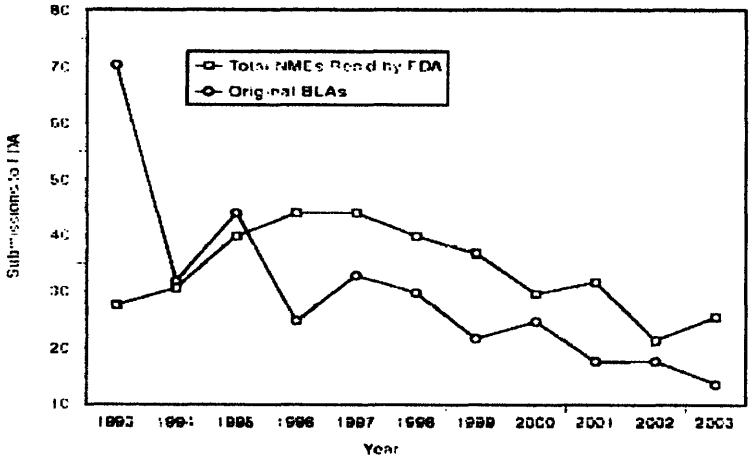
1. Stronger patent protection,
2. Emergence of information technology (enabling the sharing, recording and analyzing of information),
3. Internationalization of the market place; and
4. The transient nature of many workforces, which has lead to an increased focus on knowledge management.

Increasing Importance of Licensing in Pharmaceuticals

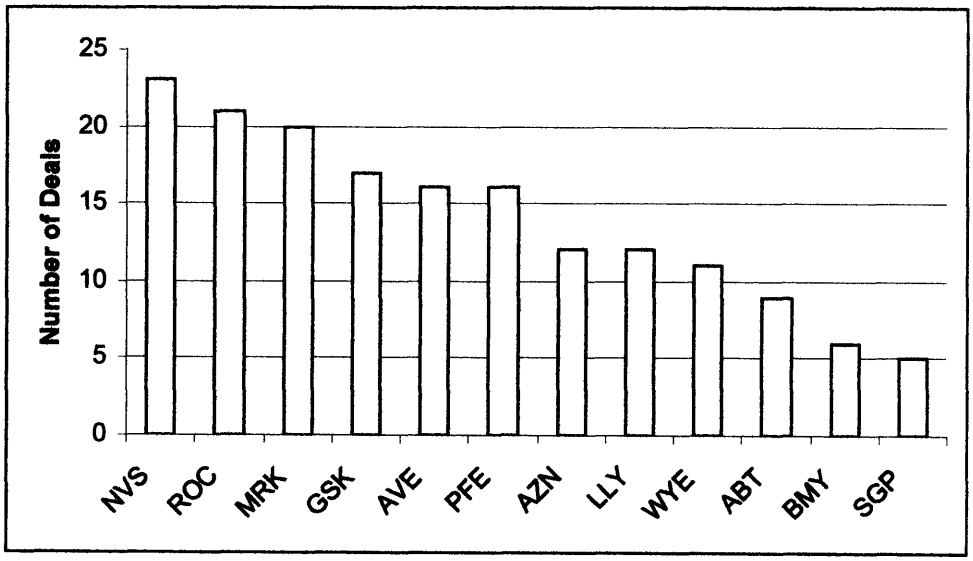
The decline in pharmaceutical research productivity, as measured by the number of new chemical entities approved per research dollar, has been well documented and cited in recent years. The following graph shows steadily increasing pharmaceutical and NIH research spending from 1993-2003 (FDA 2004). Over that ten-year period, pharmaceutical spending on research more than doubled (PhRMA 2004).



Meanwhile, the number of new approved drugs has been unimpressive. The following graph shows the number of new biological and chemical entity applications submitted to FDA over the same time period (PhRMA 2004).



Licensing provides pharmaceutical companies with a lower risk investment alternative to M&A, allowing licensees to limit and stage risk. Licensing is the most widely used form of technology transfer in bio/pharmaceuticals today. Between 1998-2002, pharmaceutical in licensing increased 60% (Demain 2004). The 20 largest pharmaceutical companies formed nearly 1,500 partnerships with biotech between 1997 and 2002 (Lam 2004). The following chart shows leading pharmaceutical licensing firms for the period March 2002-February 2003 (Demain 2004):



Even Merck, traditionally revered for its in-house R&D capabilities, has become an active licensee. From 2000-2004, Merck's partnership transactions rose almost 80%

(Bernard 2004). In-licensed products accounted for 40% of Merck's new approved drugs from 1995-2004 (Demain 2004).

According to research by Wood Mackenzie, licensed products will account for $100 billion by 2008 and will represent a third of the pharmaceutical industry's total projected revenue, up from 17% in 2001 (Hall 2004). As demand for new compounds increases, competition for viable drug candidates is getting tougher. The typical licensing deal has five pharmaceutical suitors vying for it today, as compared to three in 1998 (Bernard 2004). According to a McKinsey study, up-front payments in therapeutic alliances increased more than six-fold from 1988 to 2002, and average milestone payments soared, from $6 million in 1988-1990 to $85 million in 2000-2002 (Myshko 2004).

The supply of promising new therapeutics is expected to shrink further. A 2004 study by Boston Consulting Group estimated that the worldwide unlicensed clinical pipeline was only 1,500 compounds, with licensing demand increasing an average of 10% each year. Based on those assumptions, BCG estimated that the supply of compounds suitable for licensing will be exhausted by 2008 (BCG Focus 2004). Conversely, perhaps factors such as investments in basic science and genomics will yield a wellspring of compounds that is not yet foreseeable, however, based on current information, there will be fewer viable compounds in the near future.

Motivation for the Work

The author has been engaged as a strategic consultant to many early stage companies developing therapeutics. For most of these incipient biotech companies, strategic alliances with larger partners were a significant portion of planned financing and provided inroads to potential exits via trade sale. Despite their importance to small companies, the mechanics of strategic partnership valuations seem vague to many start-up managers.

The author was especially interested in the strategic options for a long-time early stage client developing a technology platform for cancer treatment. The company's technology could be applied to a number of solid tumor types and potentially licensed multiple times for different oncology indications or just once for all possible indications. The start-up's managers sought help with the following issues:

- Should they attempt to pursue several exclusive licenses for individual indications?
- If so, what is each indication worth?
- Would the sum of the value of the individual licenses exceed the value of one potential license?
- What is the optimal time to license the molecule(s), given potential future value increases, development cost and risks?
- Should they seek a worldwide partner or partnerships in individual regions?
- Should they partner with a large company with ample resources to commercialize the technology or with a smaller company that will dedicate more attention to the new product?

Multiple approaches, such as risk-adjusted NPV, benchmarking of similar deals and option analysis, exist to value early stage pharmaceuticals, however these methods either depend heavily on untested assumptions or vary widely in their deal value estimates. Ideally, a manager could enter the specifics of his company's molecule into an equation and receive an estimated value range.

This is clearly a naïve vision of reality, since not only do individuals' perceptions of value vary widely, each deal is impacted by human intervention: good or bad negotiators, the immediate need for new products, the desire to preclude competitors from licensing products, the need to divest an asset, etc. The following section outlines some methods currently employed to value pre-market pharmaceutical products.

Risk-Adjusted NPV/Decision Tree Analysis

Risk-adjusted NPV is probably the most widely used integrative valuation model for incipient pharmaceutical products. One begins by either estimating the total potential market size based on salient patient populations or on existing drug sales in the targeted category. An annual post-launch share is projected based on existing competition in a market, the degree of need for the emerging product, the expected intensity of the pharmaceutical sales effort and the technology's remaining patent life. One also

estimates expected direct project costs, including COGS, sales and marketing expenses and clinical development costs. Subtracting expected costs from potential revenues yields annual projected cash flows, which can be discounted back to present value.

At major product milestones, one can estimate the discounted cash flow value associated with success or failure, then probability adjust those values based on their likelihood of occurring. For instance, near the end of a product's development term, one can calculate the expected discounted cash flow associated with a successful phase III trial and product approval. Conversely, if the trial fails, the developing company will incur the discounted costs associated with all development costs between the current decision point and the phase III result. To determine value prior to phase III, The likelihood of success is multiplied by the discounted cash flows associated with phase III success and added to the product of the probability of phase III failure and discounted cash flows associated with failure.

To project value prior to FDA phase II, this composite pre-phase III value is further discounted back in time. The probability of phase II success is multiplied by the discounted pre-phase III value and added to the product of the likelihood of phase II failure and the discounted value of the costs associated with developing the product from its current state to the completion of phase II. In this way, a biopharmaceutical product's value can be estimated to its earliest stages.

Risk-adjusted NPV is an effective tool to approximate value in late stage products with well-defined markets, however, uncertainty is compounded as projects are discounted back to earlier stages. The predictive power of risk adjusted NPV is heavily dependent on accurate estimates of the following:

- Market size,
- Market share,
- Project costs,
- Project timing,
- Probabilities of success at each major milestone; and
- Discount rate (especially for a licensor attempting to assess value to a licensee).

Market-Based Methods

The primary objective of market-based methods is to value assets by studying the prices of comparable assets that have been traded between parties at arm's length in an active market (Pitkethly 1997). The primary difficulty with market-based approaches with regard to pharmaceuticals is identifying comparable molecules, given the multiple nuances of molecule type, target, indication, phase and strategic significance.

Residual Value Analysis

Residual value analysis was devised by Parr et al as an alternative method to value intellectual assets. If one has a market based valuation (either through a public stock price or recent round of financing) of the IP holding company and the company's other assets' value is easily quantified, the known asset value can be subtracted from total

enterprise value to estimate value of the asset in question (Parr et al 1988). Of course, in the case of pre-market pharmaceutical products, a potential licensor's value may be difficult to determine, as may its other assets, which are probably of equally indeterminate value as the drug in question.

Real Options Analysis

The use of real options emerged from the realization that conventional valuation techniques do not effectively account for manager flexibility and choices at multiple decision points. "Real options" analysis attempts to extend financial call and put option concepts to other ostensibly non-financial fields. A 1988 article by Mitchell and Hamilton applied real options to drug valuations, equating the cost of a pharmaceutical R&D project with the price of a call option on the future commercialization of the project and the future investment needed to capitalize on the R&D program with the exercise price of the option. The present value of the returns the company would receive from the investment could be viewed as the value of the share subject to the call option (Mitchell and Hamilton 1988).

In the context of biopharmaceutical licensing agreements, the licensee could be viewed as effectively purchasing a call option on the technology's potential. An investment in a new drug project gives one the option to continue or increase investment if things go well and to discontinue or decrease investment if things do not go well, however unlike standard financial options, the underlying asset cannot be easily traded, so real options analysis may not be applicable.

Overall, valuation of licensed drug candidates remains more art than science. Objective valuation methods exist but require substantial subjective inputs to generate estimates of value. Risk-adjusted NPV is the most widely used quantitative method and is easily understood by a range of stakeholders. Risk-adjusted NPV informed and verified by market-based approaches is probably the most accurate valuation method available today.

In addition to quantitative factors, the involvement of human business development managers necessitates consideration of qualitative concerns. Few studies have attempted to assess what licensing managers value most. The following is a discussion of one such study upon which this work is partially based.

What Matters to Licensing Managers?

In their 2002 work, Loeffler et al surveyed licensing managers to determine the factors they deemed most important to the value of a biopharmaceutical deal. The following table, from their work, shows the managers' responses (Loeffler et al 2002):

Value driver	Percentage of respondents mentioning it as important
Market, including market size for the licensing agreement, market potential, or patient population	88%
Stage—phase or stage in the development of the product	69%
Strategy, including issues of "fit" of the product in the company's pipeline and franchises, impact on the current business, and synergies	44%
Competition—competitive markets, competition from other partners for the product, and competitive products	38%
Reputation of the licensee or licensor, including inventor and management talent	31%
Investment—financial needs to develop the product	25%
Intellectual property—gaining key patents or trade secrets	25%
Novelty—innovative merit of the product (revolutionary or evolutionary)	19%
Control of the development and commercialization of a product	6%
Comparable deal valuations for similar products/technologies	6%
Reimbursement—ability or willingness of customers (payers or patients) to pay for the product	6%

The emerging drug's addressable market was cited as important by the most managers, with the stage of the molecule (affecting the degree of risk and the time to commercialization) also key to most business development professionals. In terms of objective magnitude, both market size and molecule phase are relatively easy to assess, however, synergy with the licensee's business goals, degree of competition and reputation of the licensee/licensor are more difficult to incorporate into a regression model. Surprisingly, comparable deal values, derived from aforementioned market-based approaches, were not cited as important.

Based on large unexplained variation in their regression model, Loeffler et al hypothesized that additional factors play a significant role in licensing deal values. These factors included:

- A manager's "quality", assumedly applicable to either the licensor or licensee. Effective managers could reap more value or pay less for new drugs, as appropriate,
- The pharmaceutical industry's vulnerability and willingness to pay premiums for products that could help fill their pipelines; and

- The pharmaceutical industry's willingness to pay for true innovation, not necessarily to develop these products but to prevent the competition from doing so (Loeffler et al 2002).

These additional factors almost certainly play a role, however, much of the unaccounted for variation could have been contributed by qualitative factors that were cited as important by the licensing managers but not factored into Loeffler et al's regression model, including licensor/licensee strategy, competition, reputation, investment requirements, quality of the intellectual property, control over development, comparable deal values and reimbursement issues. "Licensor/licensee strategy" is a broad and complex variable, comprising many qualitative objectives. The following is a list of major strategic licensing objectives, as described by Robert A. Myers (Myers 2001):

- Additional revenue from existing assets,
- Avoid need to invest capital in capacity,
- Avoid need to add personnel,
- Build new business with partner's know-how,
- Obtain exclusive access from supplier,
- Obtain additional talent from partner,
- Co-opt potential competition,
- Profitably divest unpromising business,
- Acquire complementary skills, know-how, channels, etc. solve patent problem; and
- Get to market faster and better

Clearly "strategic objectives" comprise a vast and non-quantifiable realm but are an essential aspect of deal value. In modern bio-pharmaceutical licensing "filling the pipeline" has become the dominant motivation. The need to have promising candidates at all stages and maintain robust growth encompasses many of the objectives cited by Myers. Unfortunately, since it is difficult to objectively assess a company's need for a product at a specific stage or in a specific therapeutic area, this work does not accurately account for company strategy, which is a major limitation.

Methodology

Identification and Exclusion of Oncology Deals

Licensing deals from 1996-2005 were culled from the ReCap (www.recap.com) database. An attempt was made to concentrate only on exclusive oncology partnerships for proprietary molecules between smaller biotech companies licensors and larger biotech or pharmaceutical company licensees. Deals with the following characteristics were excluded from analysis.

- Molecules with additional stated non-cancer indications,
- Co-marketing deals between two large companies,
- Deals for supportive care indications such as hematopoesis or pain,
- Deals in which a smaller company bought a large company's oncology asset,
- Mergers and acquisitions,
- Joint ventures,
- Deals in which a university was the licensor; and
- Partnerships involving generic compounds.

Additionally, the 2001 deal between ImClone and Bristol Myers for Erbitux was excluded. This partnership was also excluded from Loeffler et al's 2002 study due to its extraordinary size (Loeffler et al 2002).

It was believed that the market size of the molecule's target indication (e.g. lung, breast, or prostate cancer) and projected growth rate of the targeted market would be significant predictors of value. For approximately half (51) of the 101 analyzed deals, the primary oncologic indication was not available. This is because the majority of these molecules were in early stages of testing, prior to initiating human trials. As a result, regression analysis was performed using two data sets:

1) All 101 deals, including a mix of molecules with stated cancer targets and molecules in development for unknown cancer types; and
2) A sub-set of 50 deals for which a primary indication was named.

Definition of Deal "Value" and Associated Limitations

Total deal value, as published by ReCap, was used as the dependent variable for analysis. "Deal value" includes upfront cash payments, cash consideration for equity and all potential future milestone payments but excludes royalties. Total deal value was then inflation adjusted[2] and expressed in 2005 dollars. This measure is an admittedly inaccurate measure of deal value for many reasons.

- The *inclusion of payments for equity* in the smaller company is suspect because the licensee is receiving some additional consideration (assumedly the licensor's stock has some value, although most of the licensors in the database were private at the time of the deals) exclusive of

[2] Using GDP

the molecule being licensed. Deals for which equity payments were a primary component will, therefore, be overvalued in this analysis.

- The *inclusion of all potential milestone payments* diminishes the importance of FDA phase in the analysis. If milestone payments are included and treated as cash equivalents, early stage molecules may be valued as if they are already fully developed; this would lead to their values being artificially high and later stage molecules' values being artificially low since they would have relatively few milestone payments left (however, that value of milestone payments would be inherently considered due to achievement of past clinical milestones). One could attempt to adjust for this in the following manner:

  1) Identify the timing of milestone payments in each deal,
  2) Assess the probability of passing each FDA phase (using data from Tufts or other sources) and
  3) Probability adjust the milestone payments based on their associated phase and average likelihood of reaching that phase, estimate the point in the future that those payments could be made then discount them back to present value.

  Given the limited data available from ReCap[3] and the difficulty of obtaining this information from independent sources for 101 deals, this analysis was not performed.

- The *exclusion of royalties* from deal value is another major shortcoming of the study methodology. Less than 10% of deals analyzed by ReCap contained royalty information, therefore royalties were not integrated into the regression model. Royalty rates were not published with most deals and those that were listed varied widely, from 3% to as high as 50%. The focus on traditional small biotech-large biotech and small biotech-pharmaceutical company deals was an attempt to adjust for the omission of royalties, eliminating assumedly higher royalty joint ventures and co-marketing deals. Despite this, the study is certainly biased against molecules that were licensed for a high royalty, since that value is not captured.

Ignoring royalties may further diminish the impact of FDA phase, since later stage licensed products are typically expected to garner higher royalties. Guidelines published by the patent specialty firm Novelint estimate that a drug in the pre-clinical phase may receive 2-3% royalties in a licensing deal, a product licensed during in FDA human trials may receive 3-4% on future sales and an approved drug may net the licensor 5-7%

[3] ReCap lists only a total value for most deals; press releases are often attached, but these rarely specify the timing and magnitude of milestone payments. Most press releases do not state that "terms of the partnership were not disclosed".

royalties (Meyer 2001). A study of biotech royalty rates completed in 2001 reported the following average royalty rates (Medius Associates 2001):

FDA Phase	Royalty Range
Pre-clinical	0-5%
Phase I	5-10%
Phase II	8-15%
Phase III	10-20%
Market	20+%

First, it is remarkable that two sources could differ so much in their royalty rate estimates. More significant to this work, royalty rates are expected to vary widely according to FDA phase. If royalties are a significant portion of total deal value, the difference between a 0-5% royalty and a 10-20% rate is substantial; because royalty rates were omitted in this work, later stage deals should be undervalued.

Definitions of Independent Variables and Rationale for Inclusion

This work is based in large part on the analysis conducted by Loeffler et al in 2002; an attempt was made to use the variables included in the 2002 study as a baseline then add and subtract variables as was deemed appropriate. The following table shows variables that were published[4] in the 2002 work as compared to variables considered herein[5].

Variable	Included in 2002?	Included in this Work?
Licensor's previous partnership experience	No	Yes
Licensee's assets	No	Yes
Licensee is biotech or pharmaceutical	Yes	Yes
Drug is small molecule or biologic	Yes	Yes
Phase of candidate	Yes	Yes
Global or U.S. only rights	Yes	Yes
Primary indication market size	No	Yes
Primary indication growth rate	No	Yes
Year of deal	No	Yes
Novelty of molecule	Yes	No
Marketing vs. non-marketing license	Yes	No

Overall, it was thought that including additional variables could increase predictive power. "Novelty of molecule" was assessed subjectively in the 2002 study using a 1-5 scale: revolutionary products were considered most novel, receiving high scores and evolutionary products that represented incremental improvements to an existing product were rated least novel and received lower scores. More revolutionary products were associated with higher deal values in the 2002 study, especially in cancer deals, in which drugs rated "5" for novelty reaped 107% more value than drugs rated "1" (Loeffler et al

[4] Additional variables were studied but their impact was not published in the *Nature Biotech* article.
[5] The variables "cytotoxic vs. targeted", "prior year GDP" and "prior year NASDAQ value" were captured for this work but were not extensively analyzed.

2002). Novelty was not included in this study due to the difficulty associated with assigning subjective values based on very limited information.

"Marketing vs. non-marketing", captured in the 2002 work, referred to whether the licensee received rights to market the compound. This variable was not explicitly considered in this work but the exclusion of other non-traditional deals was an attempt to adjust for the nature of the partnership relationship. As a result, nearly all of the analyzed deals were "marketing".

The immediately following sections describe the rationale for inclusion of variables not addressed in the 2002 Loeffler work and general methods associated with all analyzed variables.

Previous Deal-making Experience by Licensor

The 2002 study, "Biotech-Pharmaceutical Alliances as a Signal of Asset and Firm Quality" by Nicholson, Danzon and McCullough had a significant impact on this work. Nicholson et al studied the impact of previous pharmaceutical alliances on an early stage biotech company's valuation, demonstrating that biotechs that have signed previous deals receive higher valuations from venture capitalists and public equity markets. Additionally, the authors found that biotech companies that have entered into previous partnerships receive higher average deal values in subsequent partnerships (Nicholson et al 2002).

Nicholson et al attributed the discount that early stage biotech companies receive to pharmaceutical company search costs: significant resources are expended to identify and evaluate new biotech companies. In their analysis the authors found that first time licensors received a 60% discount; the average discount for second-time licensors was 30% (Nicholson et al 2002). Based on these results, it was hypothesized that the licensor's partnership experience would have an impact on the regression model.

In this work, previous licensing experience was assessed by evaluating the licensor's previously published ReCap deals. Previous deals with universities and deals that conferred access to drug discovery technology were not counted as previous experience. For the regression model, companies were divided into two classes: 0-2 previous deals and 3+ previous deals.

Licensee Assets

In the 2002 Loeffler evaluation of licensing deal values, the identity (pharmaceutical or biotech) of the licensee was a significant factor in deal valuation, probably because it served as a proxy for company size. In this work it was hypothesized that, due to the maturation of some active licensing large biotech companies, the licensee's identity would not be nearly as significant. As a result, licensee assets at the end of the year prior to the analyzed deal was captured and included in regression analysis. Licensee assets were evaluated using historic data from Yahoo! Finance.

Licensee Identity
Larger licensee companies were coded as "biotech" or "pharmaceutical" based solely on ReCap's classification. All of the small licensor companies were biotechs.

Molecule Type
Molecule type, either biologic or small molecule was coded according to ReCap's classifications: all vaccines were considered "biologics" for regression purposes, however, independent descriptive statistical analysis was conducted for vaccine products to identify salient trends.

Molecule Phase
Drug phases were initially coded in six classes: discovery phase, pre-clinical phase, FDA Phase I, Phase II, Phase III and Market/Phase IV according to ReCap's disclosure of each molecule's phase at the time the analyzed deal was signed. The following table shows deal value by phase in the primary regression model:

Phase	# of Deals	Mean Value	Std Deviation
Discovery	18	$84.28	$72.35
Pre-Clinical	26	$75.83	$89.25
Phase I	16	$145.98	$172.30
Phase II	22	$64.78	$121.22
Phase III	17	$158.90	$140.34
Phase IV/Market	4	$91.00	$59.36

One would expect that value would increase steadily as compounds meet FDA milestones. The standard deviations indicate suggest that other factors (such as inaccurate measurement of deal value or the existence of a few large outlying deals are at play. Ostensibly, these findings are surprising, however these results echo those of Nicholson et al and Loeffler et al. The following table is from Nicholson's 2002 study (Nicholson et al 2002).

	Preclinical	Phase 1	Phase 2	Phase 3
Mean observed deal payment (millions of 1996 dollars)	$27.00	$29.40	$37.70	$33.00
Number of deals	334	43	66	80

In an effort to account for molecule phase in the regression model, the six captured FDA phases were re-organized into three arbitrary "stages":

- Discovery & Pre-clinical studies = Stage I
- FDA Phase I & Phase II = Stage II
- FDA Phase III & Marketed products = Stage III

This classification system yielded the following mean deal values.

"Stage"	FDA Phases	# of Deals	Mean Value

I	Discovery & pre-clinical	10	$66.6M
II	Phases I & II	22	$70.1M
III	Phase III & Market	18	$123.5M

Global or U.S.-only Rights
Deals were coded according to ReCap's statement of the scope of rights granted. Nearly all of the analyzed partnerships granted global rights.

Market Size & Project Growth Rate
Most discounted cash flow analysis of drug values begins with the addressable market size of the drug's primary indication. Similarly, the future growth potential of a drug market is considered an important future value determinant. It was hypothesized that market size and projected growth rate would, therefore, be significant predictors of value. Additionally, Loeffler's 2002 work found that market size was key factor for the largest percentage of licensing managers, cited by 88% of surveyed managers (Loeffler et al 2002).

Ideally, market size and growth rate data for all indications would be gathered from the same source and year. Since the analyzed data set spans ten years, determining the appropriate year for which to capture market size is problematic. One could argue that a time point in the middle of the data set would be ideal. 2001 was chosen because a 2001 Frost and Sullivan report that analyzed most cancer markets was available for free to the author. The following are market sizes and projected growth rates that were employed in this work.

Cancer Indication	Number of Deals	2001 Worldwide Market Size ($M) (Frost & Sullivan 2001)	2001-2011 Projected CAGR (Frost & Sullivan 2001)
Non-small-cell Lung	3	1,360	17.9%
Prostate	8	2,498	0.8%
Breast	7	3,280	13.5%
Colon	3	660	12.9%
Ovarian	4	637	7.4%
Non-Hodgkins Lymphomas	9	229	14.4%
Leukemias	7	99	1.2%
Pancreatic	3	227	3.1%
Melanoma	4	184	8.1%
Bladder	2	237	6.5%
Brain	1	37	9.1%

Additionally, there were two deals for bile duct cancer and head and neck cancer. Due to the low prevalence of these cancers, Frost and Sullivan did not estimate market size or project 10-year growth rates. For bile duct cancer, market size was estimated based on a percentage of the published colon cancer market. Annual U.S. incidence of bile duct cancer is 4500 new cases, compared to 148,000 new colon cancer cases (American

Cancer Society)[6]. The market for bile duct cancer was, therefore, derived by multiplying this incidence ratio (.03) by Frost and Sullivan's estimated $660M market for colon cancer. The result was a $20M market size for bile duct cancer. Frost and Sullivan's projected market growth rate for colon cancer was also applied to the one deal involving a treatment specified for bile duct cancer.

The market for head and neck cancer was estimated based on the ratio of its U.S. incidence to the U.S. incidence of brain cancer. There are approximately 40,000 new cases of head and neck cancer diagnosed in the U.S. each year, compared to 17,000 new brain cancer cases (American Cancer Society). The market for head neck cancer was, therefore, entered as $87M; the growth rate employed was 9.1%, the same as for therapies to treat brain cancer.

These market sizing methods are admittedly inexact, however, the objective was not to distinguish between a $30M market and a $37M market, but to distinguish between a $30M market and a $2B market.

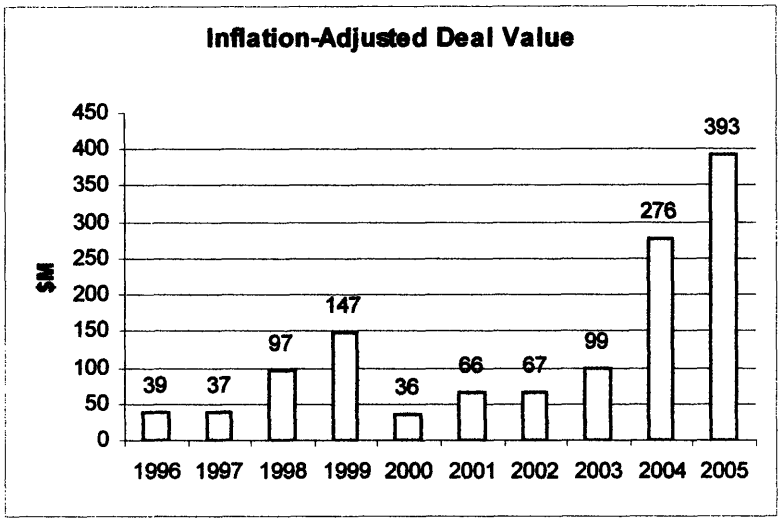
Primary indication(s) were defined by ReCap or by press releases linked to the analyzed deals. The total deals by indication listed above exceeds 50, the size of the indication-specified data set. This discrepancy is due to three incipient drugs that were in trials for multiple indications. In these cases, market sizes for the multiple indications were summed and growth rates were averaged.

Year of Deal

Although all deal values were inflation indexed, it was hypothesized that more recent deals would still earn higher values, due to the aforementioned increase in licensing competition. The typical licensing deal has five pharmaceutical suitors vying for it today, as compared to three in 1998 (Bernard 2004). According to a McKinsey and Company study, up-front payments in therapeutic alliances increased more than six-fold from 1988 to 2002, and average milestone payments soared, from $6 million in 1988-1990 to $85 million in 2000-2002 (Myshko 2004).

The following graph shows average inflation-adjusted deal value by year, demonstrating a clear increase:

[6] These are U.S. estimates; although the ratio of bile duct cancer to colon cancer may be significantly different worldwide, the purpose of this exercise was to attribute a subjectively appropriately small market size to bile duct cancer, so this U.S./worldwide discrepancy is probably not material.



The year of the deal was, therefore, included in the regression model.

Cytotoxic vs. Targeted
"Cytotoxic" molecules were defined as agents that generally interfere with DNA replication or the cell cycle, such as most chemotherapies currently in use. "Targeted" molecules were associated with a named receptor target or pathway. It was not hypothesized which molecule class would earn higher deal values: the cytotoxic drugs would likely address a wider range of cancers, while the targeted therapies would likely possess a milder toxicology profile.

Previous Year U.S. GDP
It was expected that the overall state of the U.S. economy would have a significant impact on deal value. Since partnerships typically take several months to develop and consummate, it was expected that real GDP growth in the year prior to deal signing would be an appropriate, although imperfect measure of the economic climate while the parties were considering the transaction. Annual real GDP growth was obtained from the federal Bureau of Economic Analysis (BEA).

Previous Year NASDAQ Closing Value
It was expected that stock market value would be positively correlated with value. Higher stock prices could give larger licensees the ability to pay more for deals: although licensing deals are nearly always consummated in exchange for cash, increases in a firm's stock price may presage an overall expansion. Higher valuations for smaller companies could make them less desperate for licensee cash. Again, because deals often take many months to complete, the previous year's value was seen as most appropriate. Ideally, a pharmaceutical or biotech stock index would have been used, however these indices did not exist during the earlier years of the data set.

Regression Methods
Regression analysis was done using R 2.2.1. Two separate multivariate regressions were done: one for all 101 oncology deals and one using only the 51 deals with a defined

primary oncology indication. Then, each individual variable was removed to determine the impact on each model. Finally, each variable was examined in univariate regression analysis to determine its independent impact on deal value.

Results

Comparison of Two Data Sets

Regression analysis was conducted using all 101 oncology deals and also using a 51 deal subset of deals for which the primary cancer target was already defined. Of the 101 deals, the mean inflation adjusted deal value was $102M, with a standard deviation of $121M. The median deal size was $56M, with deal values ranging from $1-$541M. Among the 51 deals with a pre-defined primary indication, the mean inflation-adjusted value was $86M, with a standard deviation of $107M. The median value of this dataset was $45M, with a total range of $1-$515.

Data Set	# of Deals	Mean	Std. Dev	Median	Range
All Cancer Deals	101	$102M	$121M	$56M	$1-541M
Pre-Defined Indication	50	$86M	$107M	$45M	$1-515M

The deals with pre-defined indications were, on average, much later stage than the overall data set. This is because all molecules in FDA Phase II or later must disclose and target a primary indication for efficacy trials. The other captured independent variables were similar among the two data sets. The following table shows mean values of key variables for the two data sets.

Independent Variable	All Cancer Deals	Pre-Defined Indication
% of Licensors w/ <3 deals	39.6%	36.0%
Mean Assets of Licensee	$11,638M	$10,172M
% of Biotech-Pharma Deals	60.4%	56%
% Small Molecule	37.6%	44.0%
% Discovery Stage	17.8%	8.0%
% Pre-Clinical	25.7%	12.0%
% Phase I	15.8%	12.0%
% Phase II	21.8%	32.0%
% Phase III	16.8%	28.0%
% Market	4.0%	8%
% U.S. Only	5.9%	10.0%
% Targeted vs. Cytotoxic	72.3%	72.0%

Regression Results Summary

In the overall data set of 101 deals, the variables "previous deals by licensor", "assets of licensee", "biotech/pharma licensee", "small molecule/biologic", "stage 2", "stage 3" "U.S./global" and "year of deal were able to account for 56.75% of variation in deal value. Adjusted R-squared was 52.98%, with a p-value of 6.391e-14. The Y intercept (baseline deal value) was -$20.06M, a result of the high amount of variability in the model. The following table shows the impact of selected independent variables.

Variable	Beta	Std. Error	P-Value
>2 Previous Licensor Deals	$33.91M	$18.26M	.06652
Prev. Years' Assets of Licensee	$4.291M per $B in Assets	$.6288M per $B in Assets	9.18 e-10*
Licensee is Pharmaceutical	-$5.41M	$21.0M	.79727

Molecule is Biologic	$9.84M	$18.95M	.60475
Molecule is in Stage 2	$4.98M	$19.22M	.79624
Molecule is in Stage 3	$74.16M	$24.37M	.00306*
License is Global	$57.33M	$38.74M	.14234
Year	$10.28M	$3.58M	.00513

*Statistically significant at the .05 level

Overall, the the assets of the larger licensee, the stage of the molecule and the year of the deal were significant predictors of deal value at the 5% level. The licensor's previous licensing experience was nearly statistically significant.

Within the sub-set of 50 deals that had a pre-defined cancer indication, the variables "previous deals by licensor", "assets of licensee", "biotech/pharma licensee", "small molecule/biologic", "stage 2", "stage 3", "U.S./global", "year", "market size" and "market growth rate" accounted for 64.24% of variability in deal value (adjusted R-squared of 55.07%, p-value=9.612e-06). The Y intercept (baseline deal value) was -$19.1M. The following table shows the impact of selected independent variables on deal value among molecules with a pre-defined indication.

Variable	Beta	Std. Error	P-Value
>2 Previous Licensor Deals	$44.92M	$22.03M	.0483*
Prev. Years' Assets of Licensee	$3.54M per $B in Assets	$.64M per $B in Assets	2.12e-06*
Licensee is Pharmaceutical	-$28.26M	$23.61M	.2385
Molecule is Biologic	$23.34M	$23.61M	.1469
Molecule is in Stage 2	-$2.24M	$29.19M	.9392
Molecule is in Stage 3	$83.93M	$33.38M	.0162*
License is Global	$46.26M	$38.65M	.2386
Year of Deal	$9.52M	$4.34M	.0343*
Mkt. Size of Indication	$13.45M per $B in Mkt Size	$7.05M per $B in Mkt Size	.0637
Proj. Growth Rate	-$1.46M per % point in growth rate	$2.0M per % point in growth rate	.4688

*Statistically significant at the .05 level

In this smaller data set, licensee experience, licensor assets, being identified as a stage 3 molecule and the year the deal was signed were significant predictors of value.

Impact of Individual Independent Variables

Licensor Previous Deals

The partnering history of the licensor company was a significant predicator of deal value. This phenomen was presaged by Nicholson's and Danzon, who attributed the discount that young biotech companies receive to search costs incurred by their larger partners. Nicholson's and Danzon found that the average discount for first time licensors is 60%, shrinking to 30% upon the company's second deal and disappearing upon its third partnership (Nicholson et al 2002).

Among the 101 oncology drug deals, 17 of the licensor companies had not signed a previous exclusive therapeutic deal, 14 had signed one previous deal and 9 had signed 2 deals prior to the analyzed partnership. The following table shows mean deal value based on the number of previous deals the smaller licensor companies had signed.

Category	# of Companies	Mean Value
0 Prev. Deals	17	$32.2M
1 Prev Deal	14	$78.6M
2 Prev. Deals	9	$50.3M
0-2	40	$53.2M
All Other Deals	61	$134.5

The oncology deals studied did not precisely follow Nicholson and Danzon's pattern, however, the mean value of deals signed by licensors who had 0-2 previous partnerships was significantly different from the mean value of deals made by more experienced licensors (p=1.347e-14).

Licensing experience of the smaller company had an impact, although not technically statistically significant, on the overall deal value regression model. The overall model predicts that companies that had signed 3 or more previous deals receive $33.91M more than companies that have signed 2 or fewer deals (p=.06652). Among deals for compounds with a pre-defined cancer indication, having a licensor that had signed more than two previous deals increased value $44.92M; this variable was statistically significant (p=.0483).

Taken alone, experience of the licensor company is sufficient to explain 10.8% of the variation in deal value in either aforementioned model (p=.004347 and p=.0241 respectively in the two regression models). When the variable is removed, the other variables still explain 55.13% of deal value variability in the overall model and 60.43% of value changes in deals for compounds with a pre-defined cancer indication.

Licensee Assets

It was thought that the maturation of large biotech companies such as Genentech and Amgen might blunt the previously marked difference between the values of deals in which the licensee is a biotech and the value of deals in which the larger partner is classified as a pharmaceutical company. Although assets reported in the prior year is admittedly an imperfect proxy for size, this variable explained a substantial portion of variation in licensing deal value. Independent of other factors, licensee assets and deal value were 66% correlated.

In the overall regression model, a $1 billion change in licensee assets caused a $4.29M change in deal value. In the sub-set of 50 deals, each $1B in assets increased deal value $3.54M. Taken alone, licensee assets explains 43.7% of variation in deal value in the large data set (p=5.3 e-14) and 37.6% of variation in the 51 deals for molecules with pre-defined indications (p=2.24 e-6).

Removing licensee assets had a pronounced impact on overall predictive power, reducing the R-squared coefficient to .2074. Among deals for molecules with a pre-defined cancer indication, R-squared was reduced to .2109.

Identity of the Licensee Company: Biotech vs. Pharmaceutical

In the 2002 analysis conducted by Loeffler et al, licensing deal values were much higher when the licensee company was classified as a pharmaceutical company: pharmaceutical companies paid 122.8% more than their biotech counterparts (Loeffler et al 2002). The oncology deal data set ostensibly yielded a similar result: the mean value biotech licensees paid was $57M, while pharmaceutical companies paid an average of $132M. Descriptive statistics are shown in the following table.

Licensee Type	# of Deals	Mean Deal Value	Std. Dev.
Biotech	40	$57M	$67M
Pharmaceutical	61	$132M	$139M

The deal values of the two groups are significantly different (p=9.92e-58). The premium paid by pharmaceutical companies was echoed in single variable regression analysis: in the total data set, beta for pharma vs. biotech was $75M (y intercept=$57M, p value of beta=.00204). In the sub-set of deals with a defined indication, beta=$38.44 (y intercept=$65.5M, p value for beta=.21757). R squared coefficients for the regression models were .09209 and .0315 respectively.

However, when biotech/pharma was considered with the other independent variables, being a pharmaceutical company may have caused a partner to pay less for otherwise equivalent molecules. Beta for pharmaceutical/biotech in the overall regression model was -$5.41M (p=.79721). Within deals with a named primary indication, being a pharmaceutical company may be a more pronounced negative predictor of value: beta=-$28.26M (p=.2385).

The relationships were not statistically significant, however, the contradiction in data may be explained by the effect of licensee assets on the predictive power of licensee identity. When licensee assets is removed from the regression models, being a pharmaceutical licensee is again a positive predictor of deal value, significantly so in the case of the overall model. Betas for the two models were $69.07M (p=.00216) and $24.25M (p=.40160) respectively.

Removing licensee company identification had a small impact in the primary model, reducing R-squared to .5671 (from .5675). With the licensee's identity is removed, licensee assets are less of a positive influence on value: a $1B change in assets produces a $4.2M change in value, compared to a slightly different $4.3M if licensee identity is included. In the deals for molecules with a pre-defined oncology indication, removing licensee identification reduces R-squared modestly, to .6293 (from .6424). Again, the magnitude of the change in value caused by assets is mildly reduced (from $3.2M per $B to $3.5M per $B). In either deal model, licensee assets is a statistically significant predictor of value if the licensee company identities are removed.

A further interpretation of the relationship between licensee company type, company size (as measured by assets) and deal value could be that, on the whole, pharmaceutical companies pay more, but they are, in general, larger as measured by assets. Very large biotech companies may actually pay more than their pharmaceutical company peers.

Impact of Small Molecule or Biologic

For purposes of the regression analysis, cancer vaccines were classified as biologics. No significant difference was found in mean deal value between the small molecule, biologic and vaccine groups or between the small molecule and biologic groups. The following table shows descriptive statistics for the three groups.

Molecule Type	# of Deals[7]	Mean Deal Value	Std. Dev
Small Molecule	38	$116.3M	$153.0M
Biologic	48	$87.8M	$89.9M
Vaccine	13	$83.5M	$95.2M

In the primary regression model, biologics may have had slightly higher values (Beta=$9.8M, p=.60475). Among deals for molecules with a pre-defined cancer indication, biologics may have been worth $32.34M (p=.1469) more than small molecules. Small molecule vs. biologic had nearly no predictive power when considered independently (R-squared=.01004, .02286 in the sub-set regression).

In the overall model, removing the variable has a negligible impact on the model, decreasing multiple R-squared to 56.62% (from 56.75%). Among deals for molecules with a pre-defined cancer indication, R-squared decreased to 62.23% (from 64.24%).

One could formulate multiple conflicting hypotheses regarding the relative values of biologics and small molecules. Some possible influences on value include:

- The difficulties associated with formulating and manufacturing biologics, which would decrease value relative to small molecules,
- The relatively mild safety profile of biologics, which could increase their value; and
- The relative freedom from post-patent expiration generic competition that biologics enjoy; this factor would also increase their value relative to small molecules

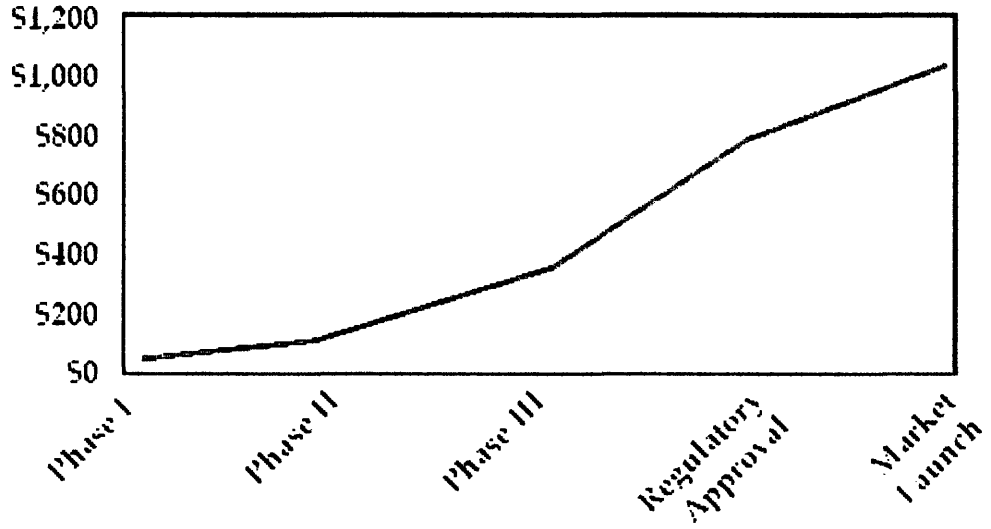
The 2002 study led by Loeffler found that small molecules, on average had 50.6% higher deal values, however, among cancer deals, small molecules were worth less than biologics, reducing value 7.3% (Loeffler 2002).

Overall, the compound's molecular identity had little or no impact on value in this work.

[7] Total N=99, does not include two deals that were classified as both "small molecule" and "biologic"

Stage of Molecule

Intuitively, phase of a drug candidate should be an important, perhaps the most important predictor of value, all other factors held constant. The following graph presents results of a 2002 study of Canadian biotechnology company values; the overall value trend and inflection points are consistent with industry expectations (Webster et al 2002-figures below are $M).



In this current work, the effects of molecule phase on deal value were underwhelming, echoing the results of Loeffler et al. Loeffler's 2002 study found that, on average, Phase IV deals were worth 21.5% more than discovery or pre-clinical stage deals, only 20.7% more in cancer. The previous work by Nicholson et al. had similar findings. The following table was presented in their 2002 paper, based on data gathered from the Windhover database (Nicholson et al 2002).

	Preclinical	Phase 1	Phase 2	Phase 3
Mean observed deal payment (millions of 1996 dollars)	$27.00	$29.40	$37.70	$33.00
Number of deals	334	43	66	80

In an attempt to effectively factor FDA phase into the model, the variable, which was initially captured in five different categories, was divided into three stages. With this alteration, molecule stage does have some influence over deal value. The following beta values for the complete data set are expressed in terms of deviation from "stage 1" deals.

"Stage"	FDA Phases	# of Deals	Mean Value	Beta	P Value
I	Discovery & pre-clinical	44	$79.3M	-	-
II	Phases I & II	38	$99.0M	$6.3M	.75220
III	Phase III & Market	21	$146.0M	$71.9M	.00549

Late stage (FDA phase III and approved) deals are clearly more valuable than deals for molecules in earlier phases. Modeled independently, stage predicts only 4.12% of deal variation (p=.0428). Removing stage from the model reduces R-squared to 48.36%.

Phase has a more significant impact on the values of deals with a defined primary indication; "stage III" deals were worth $91.3M more than "stage I" deals. The following table shows values according to stage for the indication-defined deals.

"Stage"	FDA Phases	# of Deals	Mean Value	Beta	P Value
I	Discovery & pre-clinical	10	$66.6M	-	-
II	Phases I & II	22	$70.1M	$9.0M	.7649
III	Phase III & Market	18	$123.5M	$91.3M	.0122

Independently, stage accounts for 6.088% of deal variation (p=.02164); removing stage reduces R-squared to 51.86% (compared to 56.75%) in the primary regression model and reduces R-squared to 53.59% (compared to 64.24%).

The impact of molecule phase may be partially nullified by the nature of the dependent variable being measured: "deal value" includes all future projected milestone payments. A molecule in FDA phase III will have a higher value because it is later stage, but will have very few milestone payments remaining, whereas an earlier stage but otherwise identical deal will have less current value and significant potential future milestone payments remaining that would be factored into "deal value" as measured.

Global vs. U.S.-only Rights

Deals in which rights were granted only to Europe, Asia or Japan were excluded; analysis was limited to deals for U.S.-only rights and deals for worldwide rights. One could have applied a factor to account for the size of the market accessed, however, there were too few of these deals to merit such analysis. Including deals for Europe, Asia or Japan only rights probably Of the 101 analyzed deals, 95 granted global rights and only 6 provided U.S.-only rights. The small sample size of the US-only group limited the variable's statistical power. The mean deal value for U.S.-only agreements was $71.75M; the mean value for global deals was $104.22M.

In the primary regression model, the global deals may have been worth $57.33M more than the 6 U.S. only partnerships (p=.14234). Analyzed alone, geographic rights accounted for less than 1% of deal variability. Removing the global/U.S. variable reduced multiple R-squared to 55.72% (from 56.75%). In the subset of deals with a defined primary indication, broader license scope may have increased deal value by $46.75M (p=.2386). Alone, it explained less than 1% of deal value variation. Without deal scope, R-squared is reduced slightly to 62.93% (from 64.24%).

In the 2002 Loeffler paper, scope of the rights granted was a significant predictor of value: global deals were worth 37.6% more in all indications and 85.8% more in cancer-specific deals.

Market Size & Growth Rate

Market size was estimated only for the 50 deals for which primary oncology indication was available. The variable was less correlated with value than expected, only 9.6%. Within the regression model, each $B in market size of the targeted indication caused a $13.45M change in deal value (p=.0637). Individually, market size predicts only .9193% of deal value. Removing market size reduces R-squared to 60.9% (from 64.24%).

Initial analysis indicates that growth rate of the primary indication is also slightly positively associated with deal value, with a correlation coefficient of 12%. Taken alone, growth rate has a positive effect on deal value, but explains only 1.5% of deal value variation.

As a component in the multiple regression, market growth rate may actually be negatively associated with value: each % increase causes a $1.42M decrease in deal value (p=.4688). When market size and growth rate are isolated as independent variables, growth rate is again positively associated with value, although the two variables together only explain 2.3% of changes in deal value.

The variable is somehow linked to licensee company assets: when assets are removed from the regression model, market growth rate assumes a positive role in the model; when the other variables (except licensee assets) are removed individually, growth rate is a negative predictor of value. This relationship probably does not merit analysis, since growth rate was not a statistically significant variable in any scenario. Removing both market size and market growth rate reduces predictive power to 63.75% (from 64.24%).

Removing both market size and growth rate reduced R squared to 60.59% (from 64.24%).

The market size and projected growth rate of a drug's target indication are putatively important factors in its value, however their importance may have been diminished in this work due to:

- Low sample size: there were only 50 oncology deals with a named indication.
- Other unknown indications: although a molecule is undergoing initial testing for a specific cancer, it may have applications in many other tumor types (especially in the case of generalized cytotoxic drugs). A drug that initially tested for a smaller market indication such as kidney cancer may have applications in treating other larger market solid tumor types such as lung or breast.
- Failure to assess extent of competition: lung cancer treatment is a large market, but there are many molecules currently in trials targeting that indication. Licensees certainly evaluate the existing and emerging drug landscape and adjust their valuations based on competitive products.

- The rise of targeted cancer therapies: although a drug candidate may ostensibly address a large market such as breast cancer, the patient population with an identifiable addressable mutation may be much lower and known from the outset, reducing a targeted therapy's valuation.

Additionally and possibly conversely, raw *current* market size may not be an accurate indicator of market potential. Genzyme has built a franchise in serving rare, previously untreatable diseases. Prior to the release of Serazyme, the projected market to treat Gaucher's disease would have been Lilliputian, however, due to few treatment options, companies can charge much more for therapies that impart a significant benefit.

Year of Deal

All deal value amounts were inflation adjusted to 2005 dollars, however, there was still a substantial increase in average deal values over the past few years. In both regression models, the impact of the year of the deal was statistically significant. In the overall model, each year added an average of $10.28M in deal value (p=.00513). Among deals with a defined indication, each year contributed $9.51M in additional value (p=.0343). By itself, year of the deal explained 15.73% (p=4.03 e-5) and 13.23% (p=.00942) of variation respectively in the two models. Removing year reduced R squared to 52.88% (from 56.75%) and 59.83% (from 64.24%) respectively.

Discarded Variables

Due to low or insignificant correlations, regression analysis was not performed using the following variables:

- Cytotoxic vs Targeted. The mean value of the 28 deals classified as "cytotoxic", not associated with a specific biologic pathway, was $105.46M. The mean value of the 73 "targeted" molecules was $101.08M
- Previous Year GDP. GDP in the previous year was actually negatively correlated with deal value.
- Previous Year NASDAQ Value. The value of the NASDAQ index as of December 31st of the previous year was also negatively correlated with deal value.

The following summary table shows the independent impacts of individual variables and the effects of removing variables from the larger regression model.

Variable	Independent Predictive Power	Reduction in R-Squared if Removed
>2 Previous Licensor Deals	10.80%	3.24%
Licensee Assets	43.7%	32.14%
Pharma vs. Biotech	9.21%	.62%
Biologic vs. Small Molecule	1.00%	.04%
Stage	6.09%	3.63%
Global vs. U.S. only	0%	.77%

To summarize, assets of the licensee company was the most significant driver of deal value. The following table shows impacts of individual variables and the effects of

removing variables from the regression model for molecules with a pre-defined oncology indication.

Variable	Independent Predictive Power	Reduction in R-Squared if Removed
>2 Previous Licensor Deals	10.80%	5.03%
Licensee Assets	37.60%	21.09%
Pharma vs. Biotech	3.15%	1.99%
Biologic vs. Small Molecule	2.29%	1.70%
Stage	6.09%	10.45%
Global vs. U.S. only	0%	.50%
Market Size	.92%	3.29%
Market Growth Rate	1.50%	1.09%

Licensee assets was again the most significant predictor of value, however, molecule stage took on more importance in the group of deals with a defined indication.

Study Limitations & Recommended Future Research

Failure to consider molecules' qualitative characteristics

Unlike the 2002 work of Loeffler et al, "novelty" of the molecule was not assessed as an independent variable in this work. Novelty was previously defined as the molecule's uniqueness in its space: is it a first-in-class drug or "me too" product?

Perhaps more important than molecule novelty is molecule quality, which is significantly more difficult to assess. Commercial success in the pharmaceutical marketplace is only mildly affected by the independent variables considered in this work; more important are qualitative factors such as molecule half-life, side effects and efficacy. A 2003 McKinsey and Company study found that, in addition to ligand efficacy relative to its target, safety and convenience were the key drivers of commercial value (Christensen et al). For future regression modeling, it may be possible to assemble a team to evaluate qualitative attributes, but is probably not practical to undertake an extensive process for each molecule since there is limited potential financial gain from developing a deal regression model.

Inclusion of Future Deal Payments

This weakness has been oft referenced in this work and is the probably its single greatest limitation. Ideally, one could select only deals for which there was complete information with regard to the timing and magnitude of all milestones. These payments could be probability adjusted based on accepted chances of passing clinical milestones and then discounted back to present value. Due to the dearth of deals for which there is detailed future payment history, one could not be restricted to a single indication such as cancer and still include a statistically significant number of deals. Additionally, selecting only deals with published milestone payments may bias results in an unknown way.

Inability to Assess Companies' Strategic Objectives and Competition for the Deal

Business development managers' motivation to make a deal is certainly an important, unaccounted for variable in this analysis. In addition to myriad potential strategic considerations, the number of other companies interested in a molecule would probably also impact deal value. These variables cannot be evaluated without interviewing the business development managers who constructed the analyzed licensing deals. One could attempt to interview many of the actors, however, this strategy would be difficult if using a dataset that spans ten years.

Conclusions

A comprehensive regression model to describe the values of licensing deals for oncology drugs or compounds for any other indication remains elusive. An ever-expanding array of licensing payment types makes it difficult to even determine the value of a single deal, much less quantify the impact of independent factors on collective licensing deal value.

This work was able to predict 56-64% of deal value variation and found significant associations between value and the phase of the molecule, the size (measured by assets) of the licensee partner and the experience of the licensor. The finding that licensors with less experience receive value discounts for their drug candidates may be especially controversial: business development directors at two licensing directors at large bio-pharmaceutical denied that they pay newer companies less. An alternative explanation is that, although applying a discount may not be a conscious decision by large companies, new small licensors may under-price their incipient drugs; perhaps identifying this bias may cause them to demand fair value in the future.

The principals of risk-adjusted NPV that are regularly employed in new drug valuation could be used to improve licensing deal value regression modeling: by probability adjusting future milestone payments and discounting them back to present value, one could obtain a more accurate estimate of deal value. Unfortunately, information regarding the timing and magnitude of future payments is usually not available until those milestones are met.

Ultimately, attempts to quantify licensing deal values will fall somewhat short, since non-quantitative factors greatly influence licensing decisions. Strategic goals, personalities and varying negotiating skills will ensure that drug licensing remains, in some respect, a qualitative art. Based on conversations with corporate licensing managers, the key to obtaining optimal value for a new drug, whose fundamental characteristics are already well defined, is finding the partner who needs it most at that time.

As licensing of drug candidates becomes, as is predicted, increasingly more competitive, the need for valuation techniques could actually be less acute. An increase in the number of bidders for individual compounds could cause license pricing to approximate an auction, reducing uncertainty regarding the market value of drugs. Of course, companies would still need to estimate a candidate's internal value to them to ensure that the market price is worth paying.

Licensing, as compared to more traditional acquisition, is still in its infancy as a science. As companies continue to seek to reduce risk or share rewards via licensing deals, perhaps new financial tools will emerge in licensing as currently rule in M&A analysis.

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