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Abstract

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Biotech-Pharmaceutical Alliances as a Signal of Asset and Firm Quality*

We examine the determinants of biotech-pharmaceutical alliance prices to determine whether the market for alliances is characterized by asymmetric information. We find that inexperienced biotech companies receive substantially discounted payments when forming their first alliance. A jointly developed drug is more likely to advance in clinical trials than a drug developed by a single company, so the first-deal discount is not consistent with the drug's subsequent performance. Biotech companies receive substantially higher valuations from venture capitalists and the public equity market after forming their first alliance, which implies that alliances send a positive signal to prospective investors.

I. Introduction

Biotechnology companies rely heavily on strategic alliances with pharmaceutical companies to finance their research and development (R&D) expenditures.[1] In 1998, for example, biotech companies raised three times as much ($6.2 billion) from alliances with pharmaceutical companies as from the private and public equity markets combined (fig. 1). The share of biotechnology financing raised through alliances varies with the state of equity markets. For example, in 1994, 1995, 1997, and 1998, when biotech stock prices were relatively low, biotech companies raised more money from pharmaceutical alliances than from all other sources combined. However, the continual flow of

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1. In this paper when we refer to a "biotechnology company," we use the definition common among industry practitioners: a firm that develops and markets drugs and was founded after Genentech (1976). Genentech was the first company that aspired to produce biologics (therapeutics derived from molecules present in the human body) rather than the chemical compounds being developed by established pharmaceutical firms. In practice, many biotech companies develop both biologics and chemical compounds, as do most large pharmaceutical firms. In our empirical work, we try to distinguish biologics from chemical compounds.

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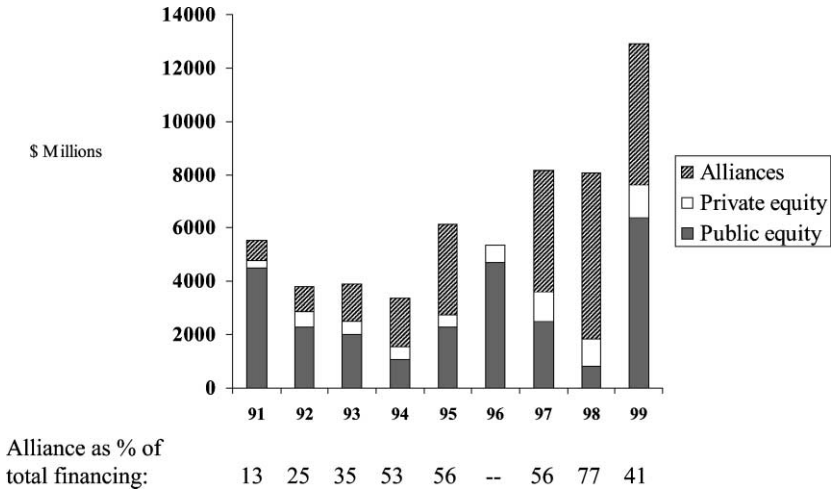

FIG. 1.—Sources of R&D financing at biotechnology companies (Source: Lerner and Merges 1998; National Science Board; Recombinant Capital; Burrill & Company). Data on Alliance financing were not available for 1996.

alliances, even in years when the public equity windows are "open," such as 1999, suggests that alliances with pharmaceutical firms create value rather than functioning merely as a source of financing.

Considerable theoretical work has been done in the economics and strategy literature examining why firms enter joint ventures (summarized by Kogut 1988). The basic theory of the firm implies that firms form alliances when other firms have comparative advantage in certain functions. In the case of the biotech-pharmaceutical industry, biotech firms pioneered new drug discovery technologies, which rely on microbiology and genomics, whereas traditional pharmaceutical companies have superior expertise in chemistry, which is essential for formulating drugs from the lead compounds generated by drug discovery. Pharmaceutical companies generally are larger, have more experience, and possibly economies of scale and scope in conducting clinical trials for safety and efficacy, navigating the Food and Drug Administration (FDA) approval process, manufacturing, and marketing and sales. Biotech-pharmaceutical deals thus may be a vehicle through which firms exchange services, given their different skills and expertise.

Large pharmaceutical companies rely increasingly on alliances to supplement their drug pipelines. Of the 691 new chemical entities approved by the FDA between 1963 and 1999, 38% were in-licensed (DiMasi 2000) In figure 2, we report the number of biotech alliances signed by the 20 largest pharmaceutical firms between 1988 and 1998.[2] The average

2. The data in figure 2 are from Recombinant Capital and include certain types of deals (e.g., platform technology deals) that are excluded from the sample used in our regression analysis. The number of deals by stage in figure 2 is therefore different from table 1.

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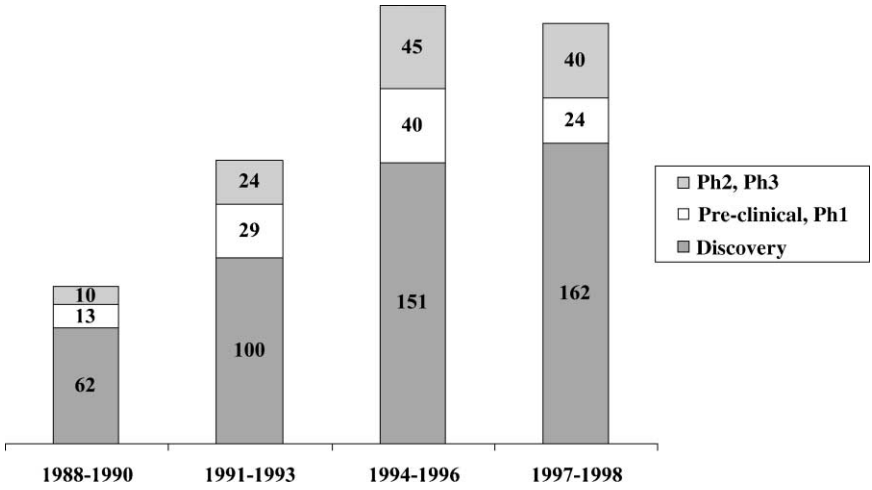

FIG. 2.—Number of biotech alliances by phase and year for the 20 largest pharmaceutical companies (Source: Recombinant Capital RDNA database).

number of biotechnology alliances signed per pharmaceutical firm per year increased from 1.4 in 1988–90 to 5.7 in 1997–98. Early-stage (discovery) deals far outnumber deals for compounds in later stages of development. In 1997 and 1998, for example, discovery deals outnumbered middle-stage (preclinical and phase 1) deals by 7 to 1, and late-stage (phase 2 and phase 3) deals by 4 to 1. The preponderance of early-stage deals may reflect the fact that there are simply more products at early stages, before attrition for scientific or economic reasons. However, the preponderance of early-stage deals is also consistent with the hypothesis that the incremental value from codevelopment is greatest if alliances are formed early in a drug's life.[3]

An alternative, not mutually exclusive body of theory focuses on imperfect information and the role of financial intermediaries that can evaluate and signal to markets the quality of firms (Leland and Pyle 1977; Campbell and Kracaw 1980; Chan 1983; Chemmanur 1993; and Chemmanur and Fulghieri 1994). Pharmaceutical firms can be viewed as performing a similar validating function. If investors (venture capitalists and investment bankers) have less information than pharmaceutical firms regarding the likely success of a biotech firm's products and the quality of its science and management, then by doing a deal with a pharmaceutical

3. The greater number of late- over middle-stage deals and their relatively low payments is a puzzle (see Longman and Roche 1997). One possible hypothesis to explain this apparent bias against middle-stage deals is that corporate structures lack a "champion" for middle-stage deals. If such bias persists, it implies a significant, unexploited profit opportunity for companies that seek out undervalued middle-stage deals. However, the conclusions on bias in payment levels do not factor in differences in costs and risks by stage of deal, and recent trends suggest that any prior bias may no longer exist. These issues are the subject of ongoing work.

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firm, a biotech firm can signal its quality to financial markets. If so, inexperienced biotech firms that can benefit most from such validation should be willing to pay for it by accepting discounted alliance payments, to be recouped by a subsequent increase in their market valuation when they next raise private or public equity capital.

Previous literature on biotech-pharmaceutical alliances has been largely empirical and provides mixed evidence on the extent of imperfect information. Lerner and Merges (1998) examine the allocation of property rights in biotech-pharmaceutical alliances, testing the theory developed by Aghion and Tirole (1994), who argue that property rights (e.g., responsibility for managing the clinical trials) should be assigned to the R&D firm when the marginal impact of its effort on the product's value is greater than the marginal impact of the licenser firm's financial investment. Lerner and Merges find evidence that biotech firms with more financial resources retain a relatively large amount of the property rights, which is consistent with efficient allocation of rights. However, Lerner and Tsai (2000) find that deals signed during periods when it is difficult for biotech firms to raise public or private equity assign more property rights to the licensee (usually a pharmaceutical firm), and these alliances are less likely to lead to a drug approved by the FDA. This suggests inefficiency in the allocation of rights, presumably resulting from imperfections in the market for financing biotech deals.[4] Pisano (1997) finds that drugs developed by biotech-pharmaceutical collaborations are less likely to reach the market than drugs developed by a single firm, which leads him to conclude that biotech companies use their informational advantage to outlicense low-quality products. This suggests a persistent information asymmetry between biotech and pharmaceutical firms leading to a lemons phenomenon in the market for deals.

None of these previous studies has examined how the magnitude of biotech-pharmaceutical deal payments vary with the characteristics of the product, characteristics of the buyer and seller firms, and the state of equity markets—the principal alternative source of financing biotech R&D. Furthermore, we are aware of no studies that examine whether deals increase the market value of biotech firms, as suggested by a model of asymmetric information and signaling.

The objective of this paper is to determine whether the market for deals between biotech and pharmaceutical companies demonstrates evidence of asymmetric information and, if so, to examine the nature and magnitude of any biases. We begin by examining the association between deal payments, measured by total precommercial payments for in-licensed drugs, and characteristics of the product (e.g., stage of development) and rights

4. An efficient approach would presumably adjust the size of deal payment, not the allocation of rights, if relative bargaining power shifts; however, this assumes that financing is available from other sources at an appropriate risk-adjusted rate.

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transferred; characteristics of the parties to the transaction, such as the biotech firm's prior experience negotiating deals; and the expected cost of alternative financing.

We then examine the effect of deals on the valuation of biotech firms in subsequent rounds of venture capital and public equity financing. If pharmaceutical firms are better able than the financial markets to evaluate the scientific and managerial expertise of private biotech companies, then biotech firms that sign deals should receive higher valuations than otherwise similar firms that develop their drugs independently, due to the positive signal provided by an alliance with an established pharmaceutical firm.

In our final analysis, we test for information asymmetries in the deals market by examining whether drugs that are developed in a biotech-pharmaceutical alliance are less likely to succeed in clinical trials than drugs developed by a single biotech firm. If so, this would tend to confirm the "lemons" hypothesis suggested by Pisano's (1997) findings: biotech firms exploit their information advantage about the quality of their drug candidates by out-licensing to pharmaceutical firms those that have relatively poor prospects.

Our main finding in the analysis of deal prices is that biotechnology companies signing their first deal receive a 47% discount relative to firms that have signed at least two prior deals, controlling for product characteristics and some measure of rights transferred, and that this discount is not consistent with the postdeal performance of the drug. Thus, unlike Pisano (1997), we find no evidence that out-licensed products are lemons. The market valuation analysis shows that biotechs are able to recoup most of this first-deal discount in subsequent financing rounds. The discount for inexperience declines to 28% on a biotech firm's second deal and is insignificant for subsequent deals. These findings are consistent with asymmetric information in financial markets, such that pharmaceutical companies are better able than money managers to evaluate the scientific and managerial expertise of private biotech firms. However, the fact that alliances occur even between well-established biotech and pharmaceutical firms suggests that signaling is not the sole function of biotech-pharmaceutical alliances; deals, on average, create positive incremental value due to the exchange of different skills. We attempt, to the extent possible, to distinguish the signaling and the value-added motivation for deals.

II. Models of the Market for Deals between Biotech and Pharmaceutical Companies

A. Perfect Information: The Gains-from-Trade Model of Deals

To provide a benchmark for deal valuations where information may be asymmetric, it is helpful to begin by characterizing a well-functioning

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market for deals, which includes many potential sellers (usually, and hereafter, biotech companies) of promising drug candidates, many potential buyers (usually, and hereafter, pharmaceutical companies) for any drug candidate; symmetric and unbiased information regarding the quality of the drugs and partnering capabilities of firms, among biotech companies, pharmaceutical companies, venture capitalists, and other money managers; and no liquidity constraints, so that biotech companies can raise sufficient capital at appropriately risk-adjusted rates. Under such conditions, potential buyers and sellers separately calculate the value of a drug as the discounted present value of its expected cash flows.

The expected net present value (V_0) of a drug currently in the preclinical stage (0), assuming that it will be developed by the biotech company that originated the drug, is

$$[V_0|d=0]=\frac{p_0p_1p_2p_3R}{(1+r)^4}-\left[C_0+\frac{p_0C_1}{1+r}+\frac{p_0p_1C_2}{(1+r)^2}+\frac{p_0p_1p_2C_3}{(1+r)^3}\right], \quad (1)$$

where the subscripts 0, 1, 2, and 3 refer to the preclinical, phase 1, phase 2, and phase 3 development stages, d is an indicator variable that equals 1 if a drug is developed jointly by a biotech and pharmaceutical firm under an alliance, p is the phase-specific probability a drug advances from a particular stage, C is the phase-specific R&D cost, R is the value of the commercial cash flows (net of manufacturing, marketing costs, and any postlaunch R&D expenses) discounted to the first year of sales, and r is the discount rate. Each development stage is assumed to last 1 year for sake of simplicity, although in reality the mean duration varies by development stage. Values of p, C, and R may differ across firms, due to differing expertise, and may differ across therapeutic categories and types of products (e.g., biologics versus chemical compounds).

If this drug advances to phase 1, its value (V_1) becomes

$$[V_1|d=0]=\frac{p_1p_2p_3R}{(1+r)^3}-\left[C_1+\frac{p_1C_2}{1+r}+\frac{p_1p_2C_3}{(1+r)^2}\right]. \quad (2)$$

The value V_1 typically exceeds V_0 for three reasons. First, as a drug advances from discovery to clinical trials to regulatory approval, the scientific risk that it will fail safety and efficacy tests usually decreases; hence, the probability that it will be commercialized usually increases.[5] Second, projected revenues become more imminent as commercialization approaches and are discounted less heavily. Third, as a drug develops, more R&D costs become

5. The probability that the FDA will approve a drug could conceivable decrease as the drug advances if a company discovers potential side effects that are not substantial enough to merit discontinuing development but are substantial enough to cause a downward revision in the approval probability.

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sunk. Therefore, V_0 and V_1, as defined in equations (1) and (2) can be viewed as the reservation price or the minimum asking price of a seller, substituting its specific values for the parameters.

Consider now the maximum amount that a pharmaceutical company would be willing to pay for this drug, assuming that it would assume all subsequent costs. If the pharmaceutical company has the same probabilities, revenue, and cost estimates as the biotech company, V_1 also reflects the amount that the buyer-pharmaceutical company would be willing to pay for this drug in phase 1. With competitive entry into the development of drug candidates, the initial expected net present value (V_0) for the marginal drug should be zero. The expected net present value of a phase-1 product (V_1) is positive by an amount that reflects the costs and risk already incurred by the biotech company. Similarly, V_2 for a phase-2 product is higher by an amount that reflects the additional costs sunk and the incremental probability the drug will be commercialized. Thus, under the assumptions of symmetric information, the value of deals signed at successive phases should increase by an amount that reflects the incremental costs and risks incurred. This conclusion assumes no difference in assignment of rights, in the type of products involved, or in the structure of deals by stage of development.[6]

With identical costs and capabilities between firms there would be no rationale for doing deals, even with perfect information. The gains-from-trade or comparative-advantage theory of deals assumes that, if an experienced pharmaceutical firm works with a biotech company, some of the development costs will be lower or expected revenues will be higher. In particular, a pharmaceutical firm may potentially increase p due to greater experience in managing clinical trials, decrease C due to economies of scale and scope, or increase R due to its large and experienced sales force. In that case, the value of a phase-1 drug if codeveloped by the pharmaceutical firm $(V_1|d = 1)$ exceeds its value if developed solely by the biotech firm $(V_1|d = 0)$. The actual deal payment is between $V_1|d = 1$ and $V_1|d = 0$, depending on the how the incremental value of codevelopment is shared, which in turn depends on the firms' relative bargaining power.

The profit-maximizing strategy for a biotech firm is to develop a drug in-house or select a stage of development in which to form an alliance, according to which alternative yields the highest discounted present value. The gains-from-trade model predicts that a necessary condition

6. Deal payments may also vary by stage of deal if the assignment of responsibilities, rights, and costs differ by deal stage. For example, for predevelopment deals (prior to the start of human clinical trials), a pharmaceutical company may incur some or all of the costs of clinical trials and would usually bear most manufacturing and marketing costs. If the deal is signed late in phase 3, however, the biotech company has already built substantial manufacturing capability and may participate in postlaunch manufacturing and marketing, sharing some of these costs in return for a larger share of drug revenues.

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for a biotech firm to sign a preclinical deal is that the expected value of the drug in an alliance $(V_0|d = 1)$ exceeds its expected value if developed independently $(V_0|d = 0)$, and exceeds the expected value of the drug if a deal were signed at a later stage $(V_1|d = 1, V_2|d = 1,$ and $V_3|d = 1)$.[7]

In the perfect-information model, when a biotech firm signs a deal with a pharmaceutical firm, there should be no effect on the biotech's market value. Venture capitalists and other investors should have anticipated the incremental value of codevelopment when determining the company's value in the previous financing round.

B. Imperfect Information: The Signaling Model of Deals

We now relax the assumptions of a well-functioning market for biotech-pharmaceutical deals and analyze the implications of market imperfections on the type of deals, deal payments, and the performance of drugs developed in biotech-pharmaceutical alliances. Consider first asymmetric information: prospective buyers (pharmaceutical firms) and investors (venture capitalists) may have less information than prospective sellers (biotechs) regarding the quality of a biotech company's drugs and the competence of its management. This information asymmetry could be particularly severe in the preclinical phase, before empirical evidence on the drug's safety and clinical efficacy are available.

We adapt to the biotech-pharmaceutical setting a model that Campbell and Kracaw (1980) use to explain the role of financial intermediaries as signalers of high-quality firms. Specifically, we assume high-quality (H) and low-quality (L) biotech firms produce high- and low-quality drug candidates, respectively.[8] The expected discounted net present value of a high-quality drug exceeds that of a low-quality drug at all development stages $(V_H > V_L)$ due to superior scientific characteristics or superior managerial skill or effort. Biotech firms know the quality of their drug candidates but cannot convey this information credibly to pharmaceutical firms and equity investors. If there is no mechanism to signal quality, the only possible equilibrium is a pooling equilibrium: high-quality and low-quality biotech firms are both valued at $\underline{V^F}$ rather than the values commensurate with the quality of their drug portfolios, V_H^F and V_L^F. Here the superscript F refers to the firm as a whole, so V^F is the sum of the

7. This is a necessary not a sufficient condition for a deal if some potential deals fail due to disagreement over sharing the incremental value from codevelopment. It is also possible that biotech companies accept less than the value-maximizing terms on one drug to participate in on-the-job training from sharing manufacturing or marketing with an experienced pharmaceutical firm.

8. The qualitative predictions of this model would be the same if we adopted the more realistic assumption that high- and low-quality firms generate drugs from two different quality distributions rather than drugs with different discrete quality measures.

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expected value of all drugs in a firm's portfolio as determined by equity investors.

Although high-quality biotech firms would be willing to pay an amount up to $V_F^H - \underline{V^F}$ to have their quality identified, Grossman (1976) and Grossman and Stiglitz (1976) show that there may be insufficient incentives to invest in information production in markets with asymmetric information regarding asset quality. When information is a public good and incorporated instantly into the market prices of assets, the organization incurring the cost of distinguishing high- and low-quality assets cannot appropriate the benefits of information production because the values of high-quality assets rise when they are identified as such. Furthermore, even if high-quality biotech firms could make side payments to compensate the signaling firm for its costs, there remains a moral hazard problem: the signaling firm could collect the payment without actually producing accurate information unless there is an effective commitment device.

The market for deals between biotech and pharmaceutical firms appears to offer a mechanism by which biotech firms can compensate pharmaceutical firms for information production costs and pharmaceutical firms have incentives to be truthful. When pharmaceutical firms license drugs from biotech firms and agree to share the development costs and revenues, they have an incentive to evaluate the quality of the asset they are acquiring, which mitigates the moral hazard problem.[9] The market for deals also allows biotech firms to compensate pharmaceutical firms for information costs by allowing pharmaceutical firms to subtract these costs from the deal payments.

A number of theoretical studies in the finance literature examine the role of intermediaries in signaling firm quality, but to our knowledge none of the theories has been tested empirically. Leland and Pyle (1977) argue that the appropriability and moral hazard problems "can be overcome if the firm gathering the information becomes an intermediary, buying and holding assets on the basis of its specialized information." This seems to describe exactly the role of pharmaceutical firms in searching for drugs to in-license. In their model, the signal of a firm's quality is the fraction of equity retained by the entrepreneur. In Campbell and Kracaw (1980), the moral hazard problem is resolved if the information-producing intermediary has a sufficiently large stake in the market and thus incentives to invest an efficient amount in information production and report it truthfully. Chemmanur (1993) argues that high-value firms compensate investment

9. Full elimination of incentives for underinvestment in information by the signaling firm requires outright purchase of the asset, but this might increase moral hazard by the seller. The fact that deals generally stipulate that the parties share costs and revenues could be a second-best way to deter moral hazard by both parties; it also suggests that gains from collaboration outweigh the suboptimal incentives and moral hazard created by sharing contracts.

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banks for their information production costs by underpricing their initial public offering, and investment banks have incentives to generate credible information to maintain their reputation (Chemmanur and Fulghieri 1994). Finally, Chan (1983) shows that the presence of an informed intermediary can affect the quality of assets in the market and increase social welfare rather than merely redistribute wealth from over- to undervalued firms.

Applying these models, we assume that pharmaceutical firms and venture capitalists incur search costs, S, to discern a drug's expected net present value; and these costs can vary by stage of development. Pharmaceutical firms have a comparative advantage in information production due to their superior scientific and commercial knowledge relative to venture capitalists and other investors. Part of S is dedicated to identifying the competence of the biotech firm's management, since the biotech company is integral to developing the drug, and part to identifying the specific drug's quality. The former cost ise incurred only as long as it takes prospective buyers to discern a firm's managerial quality, while the latter cost occurs with each deal. We consider four scenarios regarding the incremental value of codevelopment relative to the cost of producing information and the magnitude by which high-quality biotech firms are undervalued in a pooling equilibrium.

In the first scenario, the incremental value of codevelopment for high- and low-quality drugs ($V_H|d = 1 - V_H|d = 0$ and $V_L|d = 1 - V_L|d = 0$) exceeds S, so both high- and low-quality biotech firms sign deals. If there are a large number of prospective buyers relative to sellers, high-quality biotech firms receive payments of $V_H|d = 1 - S$, and low-quality firms receive payments of $V_L|d = 1 - S$.[10] A biotech firm considered by pharmaceutical firms to be of high quality should receive higher payments from subsequent deals (relative to its first deal) because it needs to compensate the pharmaceutical firm only for the drug-specific information production costs. The number of deals required to signal a firm's quality type is an empirical question that we examine.

Although both types of biotech firms sign deals, we assume there still is a separating equilibrium, because venture capitalists can identify the quality of a biotech firm from the magnitude of the deal payment. That is, we assume venture capitalists can distinguish $V_H|d = 1 - S$ from $V_L|d = 1 - S$. As a result, biotech firms are valued appropriately (V_H^F and V_L^F) in the subsequent financing round (either follow-on venture capital financing or an initial public offering). The market value of high-quality biotech firms increases by $V_F^H - \underline{V}^F$ following a deal and the market value of low-quality biotech firms decreases by $\underline{V}^F - V_F^L$. Low-quality firms do not develop their drugs independently if venture capitalists know the

10. Later, we discuss the possibility that the gains from codevelopment may accrue wholly or in part to the pharmaceutical firm, if there are few buyers relative to sellers, so the biotech firms receive payments of $V_L|d = 0 - S$ rather than $V_L|d = 1 - S$.

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incremental value of codevelopment is large enough to compensate a pharmaceutical firm for its search costs. If a low-quality biotech forgoes signing a deal to try to maintain its overvalued status, the venture capitalists infer the biotech firm has low-quality drugs. Knowing this, the biotech signs codevelopment deals and incurs the reduction in value.

In the second scenario, we assume that $(V_H|d = 1 - V_H|d = 0) > S > (V_L|d = 1 - V_L|d = 0)$. A pharmaceutical firm's cost of evaluating an inexperienced biotech company exceeds the incremental value of codevelopment for low-quality drugs but is less than the incremental value of codevelopment for high-quality drugs. Only high-quality biotech firms are able to compensate pharmaceutical firms for the search costs, so only high-quality firms sign deals and receive payments of $V_H|d = 1 - S$.[11] The market value of high-quality biotech firms increases by $V_H^F - \underline{V}^F$ following a deal, and the value of biotech companies that have a drug candidate but do not sign a deal falls by $\underline{V}^F - V_L^F$.

The third scenario is similar to the second scenario: $(V_L|d = 1 - V_L|d = 0) < S$; $(V_H|d = 1 - V_H|d = 0) < S$; and $(V_H|d = 1 - V_H|d = 0) + (V_H^F - \underline{V}^F) > S$. Pharmaceutical search costs are larger than the incremental value of codevelopment, but high-quality biotech firms can compensate pharmaceutical firms from the subsequent increase in value once venture capitalists receive the quality signal. As in scenario 2, only high-quality firms sign deals and firms are correctly valued at the next financing round. Note that capital market imperfections may prevent high-quality biotech firms from borrowing enough money to compensate pharmaceutical firms for their search costs, preventing the formation of alliances.

In the final scenario, no deals are signed because $(V_L|d = 1 - V_L|d = 0) < S$; $(V_H|d = 1 - V_H|d = 0) < S$; and $(V_H|d = 1 - V_H|d = 0) + (V_H^F - \underline{V}^F) < S$. Although this scenario is clearly not borne out in the market because we observe many deals, it highlights another way that information costs could affect the market for alliances. In scenarios 2 and 3, low-quality biotech firms continue to develop their drugs independently rather than sign deals due to the high information costs. It is possible that the cost to pharmaceutical firms of identifying the quality of a drug (and the quality of a biotech firm) might be substantially smaller once the drug has completed phase 1 or phase 2 trials and more information is available. For example, consider a situation where $(V_{L,0}|d = 1 - V_{L,0}|d = 0) < S_0$ when a drug is in the preclinical stage, but once the drug reaches phase 2 trials, $(V_{L,2}|d = 1 - V_{L,2}|d = 0) > S_2$, where the subscripts 0 and 2 refer to the preclinical stage and stage 2, respectively.

11. The payment to the biotech firm may be somewhat less than $V_H|d = 1 - S$ if the pharmaceutical firm has to incur some search costs to determine that a firm or product is of high value. The lower payment to high-quality firms would compensate the pharmaceutical firm for the risk that a firm will turn out to be of low quality.

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In this case, we expect the quality of drugs involved in later-stage deals to be lower than the quality of drugs involved in preclinical deals. Later-stage deal payments appear to be biased downward in a naïve analysis, but this is due to unmeasured quality. This model predicts that companies signing their first deal on a late-stage drug receive relatively low payments due to low unmeasured quality.

In the empirical analysis, we attempt to identify whether the actual market for deals is consistent with scenario 1, 2, or 3 (with the latter two scenarios being empirically indistinguishable); scenario 4 is clearly rejected by the evidence on the number of deals. One method of distinguishing the scenarios is to examine the impact of deals on biotech company valuations. If scenario 1 prevails, both types of companies sign deals. The effect of a deal on a biotech company's valuation is ambiguous: it depends on the proportion of biotech companies that are high quality, and the magnitude of the over- versus the undervaluation. In scenarios 2 and 3, only high-quality firms sign deals, which causes investors to bid up the value of high-quality firms from $\underline{V}^F$ to V_H^F. Thus, a positive relationship between a deal and subsequent appreciation in a company's value is a necessary but not sufficient condition to prove the relevance of scenario 2 or 3.

Another way to distinguish scenario 1 from scenarios 2 and 3 is to examine differences in deal payments according to the stage of a drug's development. If search costs exceed the benefits of codevelopment for at least some firms, low-quality drugs are more likely to be out-licensed at later stages of development, when information costs are relatively low. Deal payments involving drugs in later stages of development therefore are relatively low due to unmeasured drug quality. The data prevent us from testing this hypothesis conclusively, but we present some tentative evidence.

In all scenarios of the signaling model, payments to a biotech firm for its first deal (and possibly later deals) are relatively low, to compensate the pharmaceutical firm for information costs. An alternative, and not necessarily mutually exclusive, explanation for a first-deal discount is that biotech firms learn; codevelopment with a pharmaceutical firm adds more value for relatively inexperienced biotech firms. If pharmaceutical firms capture most of this incremental value due to bargaining power, then deal payments are relatively small for inexperienced biotech firms.

In both the gains-from-trade and signaling models, deals occur only after a pharmaceutical firm has invested in information regarding the quality of the biotech company and the drug. These models predict that there will be no lemons problem: biotech firms cannot out-license inferior products. We test this prediction by examining whether drugs out-licensed by biotech firms are less likely to complete clinical trials and be approved by the FDA relative to drugs that biotech firms develop independently.

The imperfect information model has focused on asymmetric information. Another possible imperfection is market power due to small

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numbers. Specifically, there may be few buyers relative to sellers for the numerous preclinical drugs and few sellers relative to potential buyers for late stage products, due to the attrition of drug candidates or inadequate planning by buyers. Moreover, buyers of late-stage deals may have a more inelastic demand if product failures create gaps in a pharmaceutical firm's product pipeline. If sellers have greater relative bargaining power for late-stage products, late-stage deals would have relatively high prices, even after adjusting for differences in cost and risk.

Another possibility we examine is that capital market imperfections may affect the market for deals. Deals and equity are alternative sources of financing R&D, so biotech firms should select the least expensive financing source. When the public and private equity markets are "closed," deal values may be low relative to when it is inexpensive for biotechs to raise private and public equity.

Figure 1 presents data on the amount of public and private equity raised by biotechnology companies between 1991 and 1999. Three times during this period—1991, 1996, and 1999—investors were attracted to the biotechnology industry and these companies raised a substantial amount of public equity. However, there were also periods when it was difficult or extremely costly for biotech firms to raise equity. At such times, alliances with pharmaceutical companies may be a relatively attractive way to raise money. Figure 1 supports this hypothesis: alliance funding is relatively high when total equity funding is relatively low. In years when the public equity market is tight, the supply of deals increases, and one would expect the mean deal price to decrease, other things equal. This prediction may be offset if the biotech firms are forced to sign deals on their highest-quality drugs during tight equity markets.

If imperfections in the financial markets create liquidity constraints, a biotech company with a weak balance sheet might be forced to accept early-stage offers because it lacks the financial resources to develop a drug independently. To test this, we include in the empirical analysis the financial strength (measured as the value of equity plus debt) of a biotech company. Our hypothesis is that, controlling for drug characteristics, deal payments vary inversely with the market value of the biotech company.

III. Empirical Method

A. Determinants of Deal Payments

We examine the determinants of the deal prices for drugs that are sold or licensed, usually from biotech to pharmaceutical companies, to see if inexperienced biotech firms implicitly pay pharmaceutical firms for the cost of producing information and whether prices are affected by other possible market imperfections. Equation (1) implies that deal prices must be adjusted for variations in scientific risk and development costs by stage

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of development and for expected revenues, which depend on the size and competitive structure of the target market. Using ordinary least squares, we regress the logarithm of the price (P_{ijt}) that firm j receives by licensing drug compound i in year t on product characteristics and the structure of the deal ($\mathbf{X_i}$), characteristics of the selling firm ($\mathbf{F_j}$), characteristics of the buying firm ($\mathbf{F_k}$), and characteristics of the equity market for biotech firms ($\mathbf{M}$) at the time of the deal (t):

$$\log(P_{ijt}) = \gamma_0 + \boldsymbol{\gamma_1}\mathbf{X}_i + \boldsymbol{\gamma_2}\mathbf{F}_{\mathrm{jt}} + \boldsymbol{\gamma_3}\mathbf{F}_{\mathbf{kt}} + \boldsymbol{\gamma_4}\mathbf{M}_{\mathrm{t}} + \varepsilon_{ijt} \quad (3)$$

We assume that the random disturbances (ε) are normally distributed conditional on the observed covariates, have a mean of zero, and arise because the two parties to the alliance observe drug characteristics that we do not (e.g., expected efficacy of the drug). We include in $\mathbf{X}$ indicator variables for the drug's therapeutic class (a rough proxy for market size and any other class-specific costs or risks), indicator variables for the drug's development stage at the time of the deal (discovery-preclinical, phase 1, phase 2, phase 3), and an indicator for whether the drug is a biologic product.[12] We also include separate indicator variables if the seller retained commercial rights to the drug for the U.S. or Japanese market, whether the buyer purchased equity in the seller firm as part of the deal, and reverse licensing deals.[13]

We include in $\mathbf{F}_{\mathrm{jt}}$ a series of indicator variables to measure the seller's experience, using the number of deals the seller has signed prior to the deal being examined. The coefficients on these indicator variables (e.g., biotech has signed one prior deal or biotech has signed two prior deals) in the signaling model measure the decline in S, the pharmaceutical firm's cost of evaluating a drug, as information accumulates regarding the biotech firm's managerial capabilities. In the gains-from-trade model, the experience variables measure the change in the incremental value of co-development as a biotech firm learns.

Conditional on prior deal experience, a small selling firm might be willing to accept a lower deal price if it can benefit from a positive signal associated with an alliance, particularly if the licensee is a large established firm. A large buying firm might be able to negotiate lower deal prices due to experience or specialized skills; on the other hand, a large buyer might be willing to pay higher prices to in-license drugs if there are substantial economies of scale or scope in R&D. We include firm sizes, measured as the enterprise value for public companies (market value of

12. We consider a drug to be a biologic if the originating firm focuses on large molecules or antibodies.

13. The data available to us are insufficient to estimate a complete model, which would treat the rights transferred and the stage of the drug at the time of the deal as simultaneously determined with the deal payment. We assume here that these other deal terms are predetermined. Our estimates thus reflect deal values conditional on these other deal characteristics.

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the equity plus book value of debt) and the post-money valuation at the most recent round of venture capital financing for private firms. The expected sign on the size of the buyer is ambiguous a priori.

Lerner and Tsai (2000) show that biotechnology companies transfer a greater number of property rights (e.g., control of the clinical trials) to pharmaceutical companies when it is difficult or expensive to raise money from public and private equity markets. However, a more efficient adjustment to a shift in bargaining power would be for biotech companies to accept smaller deal payments when equity financing is expensive. We include the amount of funds raised by biotechnology companies from public and private equity markets in each year, indexed relative to a base year (1996) to measure the state of the equity markets. To test whether small biotech companies are particularly vulnerable when the equity markets are "closed" or equity financing is expensive, in some specifications, we interact the equity index with the selling firm's enterprise value.

The data available on biotech-pharmaceutical company deal prices are not ideal for testing whether prices paid at certain stages of drug development are systematically biased, after controlling for costs, risks, and the characteristics of drugs. Since we lack good estimates for these parameters, our conclusions regarding bias in deal prices by stage of development are preliminary and approximate. Similarly, we lack the data to test whether biotech firms with low-quality drugs are forced to sign late-stage deals, when information costs are lower. This would require showing that deal payments for late-stage drugs are too low given the relatively high probability of reaching the market and the magnitude of sunk development costs relative to early-stage drugs. Deal payments typically include several components, including up-front payments of cash and investments in the selling firm's equity, milestone payments (payments conditional on the drug achieving certain designated events), sponsored research payments (usually a fixed amount per Ph.D. scientist assigned to perform research on the drug), postcommercial payments (usually a royalty percent of gross sales), and sometimes a "quid" in the form of rights to another product from the buyer. A complete evaluation of the deal value requires data on each of these components, the rights and responsibilities transferred and retained (e.g., territories and therapeutic categories covered), and the probabilities that contingent payments will be made.

The valuation data available to us are the total potential precommercial payments from the buyer to the seller, where *potential* refers to the scenario where all contingent payments are made. This figure thus includes up-front payments, sponsored research payments, investments in the selling firm's equity as if it were cash, and any potential milestone payments. The total potential precommercial payment excludes postcommercial royalty payments, any cost sharing, and the value of any product swaps. Since this total precommercial measure of the deal value

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incorporates milestone payments as equivalent to cash, without discounting for uncertainty or the time value of money, we expect it to be invariant by stage, except to the extent that any of the following differ by the stage of the deal: (1) the rights transferred, (2) bargaining power, (3) the absolute amount of the total deal value that is paid in precommercial versus royalty payments, and (4) the quality of products traded.

B. Effect of Deals on Firm Valuations

To test the signaling model, we examine the impact of deals on the valuations that private biotech firms receive from venture capitalists and the broader set of investors when the company goes public. Specifically, we regress the value of biotech company j after the nth round of financing (Y_{jn}) on an indictor variable that equals 1 if the company had signed one deal prior to the financing round $n(D_n^1)$, and an indicator variable that equals 1 if the company had signed two or more such deals prior to financing round $n(D_n^{2+})$:[14]

$$\log(Y_{jn}) = \alpha_0 + \alpha_1 D_{jn}^1 + \alpha_2 D_n^{2+} + \boldsymbol{\alpha_3 \mathbf{T_t}} + \boldsymbol{\alpha_4 \mathbf{N_n}} + u_{jn}, \qquad (4)$$

where the random disturbances (u) capture the value of unmeasured firm characteristics. The market value of a firm is defined as the product of its shares outstanding and the price per share at the conclusion of a private-equity financing round or at the time of the initial public offering (IPO). Separate indicators are included for the each round of venture capital financing and the company's initial public offering (n) and the year (t) in which the financing occurred. The financing round variables measure the market value of a firm's experience.

In scenario 1 of the signaling model described in Section II, the incremental value of partnering is large relative to the cost of distinguishing high- from low-quality biotech firms, so both high- and low-quality biotech firms sign early-stage deals. In this scenario, α_1 (and α_2) could be positive or negative, depending on the number of high- versus low-quality biotech firms that sign deals and the magnitude of under- and overvaluation in the pooling equilibrium that prevailed before deals were signed. In scenarios 2 and 3, only high-quality biotech firms sign early-stage deals, so α_1 measures $V_H^F - V_L^F$, the difference in the market value of high- and low-quality biotech companies once the quality signal has been received. In the gains-from-trade model, α_1 (and α_2) is predicted to be zero if the deal values on average are equal to the value of assets transferred; it is positive only if sellers on average capture some of the incremental value created by the alliance and the incremental value of the deal is not already anticipated by equity markets.

14. We adjust the standard errors to allow the errors to be correlated over time for a particular firm.

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One criticism of equation (4) is that α_1 and α_2 might not measure the incremental signal value of a deal's announcement only but also any characteristic correlated with a firm's value that is unobserved to the analyst but observed by venture capitalists. For example, firms with capable managers and scientists might produce high-quality drugs, sign deals with pharmaceutical firms, and receive relatively high valuations from venture capitalists, but this does not imply a causal relationship for the deal signal.

To focus on the incremental value of the deal announcement, we also estimate a first-difference version of equation (4) that eliminates any time-invariant, unobserved firm characteristic, such as the quality of a company's science. Specifically, we regress the percentage change in a biotech company's value between financing round $n-1$ and n on an indicator variable that equals 1 if the company signed its first deal between these two financing rounds (D^1_{j,n_n-1}), an indicator variable that equals 1 if the company signed a deal between these two financing rounds and it had already signed a deal prior to round $n-1$ (both D_{j,n_n-1} and $D_{j,n-1}$ are equal to 1), and indicator variables for the financing round and the year in which the financing occurred:

$$\log(Y_{j,n}) - \log(Y_{j,n-1}) = \beta_0 + \beta_1 D^1_{j,n\_n-1} + \beta_2 D^1_{j,n\_n-1} D_{j,n-1} + \boldsymbol{\beta_3}\mathbf{N_n} + \boldsymbol{\beta_4}\mathbf{T_t} + \eta_{jn} \quad (5)$$

We also include a continuous variable for the number of months between the successive financing rounds. A positive coefficient on the deal variable in this specification provides strong evidence that the change in a firm's market value is associated with the recently concluded deal.

C. *Drug Development Success Rates*

In the gains-from-trade model, deals are signed only if the expected value of the drug is greater if codeveloped than developed independently. In the signaling model, deals are signed only if biotech firms reimburse pharmaceutical firms for information costs. Thus, in these models, there is no lemons problem: biotech companies cannot dump their inferior products on pharmaceutical firms. We test this by examining whether drugs that biotech firms develop in alliances are as likely to advance to the next development stage as drugs they develop independently.

The probability a drug will advance to the next development stage is a function of the quality of the drug, the effort exerted by the company or companies involved in the development, and the experience of the companies involved. We assume the probability that drug i originated by company j will complete a human trial ($A = 1$), conditional on beginning the trial, is a function of drug characteristics ($\mathbf{X_i}$), the characteristics of

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the involved firm or firms ($\mathbf{F_j}$), and an indicator variable (D_i) that equals 1 if the drug is being developed in an alliance:

$$\Pr(A_{ij} = 1) = \frac{\exp(\varphi_0 + \varphi_1 \mathbf{X}_i + \varphi_2 \mathbf{F}_{jt} + \varphi_3 D_i)}{1 + \exp(\varphi_0 + \varphi_1 \mathbf{X}_i + \varphi_2 \mathbf{F}_{jt} + \varphi_3 D_i)} \quad (6)$$

A negative coefficient for φ_3 is consistent with a lemons problem in the market for deals or moral hazard, if each firm in an alliance invests suboptimal effort because it shares the benefits of their investment with the partner firm. A positive coefficient for φ_3 is consistent with either no asymmetric information and moral hazard or asymmetric information and moral hazard problems that are overwhelmed by the positive benefits of codevelopment.

We perform three separate logit regressions for drugs that begin phase 1, phase 2, and phase 3, where the dependent variable is 1 if a drug completes the trial, and 0 otherwise. We include 13 indicator variables for the drug's therapeutic class. Asymmetric information is likely to be most severe for small, relatively new biotech firms. We include in equation (6) separate indicator variables for companies that originated three or fewer drugs during our sample period, between 4 and 24 drugs, and 25 or more drugs. We also include interaction terms between the firm-size indicators and the codevelopment indicator (D_i).[15]

Some of the drugs are censored, since we do not observe the termination of projects; rather, we observe whether a drug advances to the next phase. Drugs that had not been launched by 2000, the final observation period in our data set, are right censored. To address this censoring, we calculate the maximum length of time required for drugs in our sample to complete each development stage (5 years for phase 1, 5 years for phase 2, and 4 years for phase 3). Drugs that are right censored and started a stage beyond these time periods are assumed to have failed (coded as zero); right-censored drugs that started a phase within these time periods are omitted from the regressions rather than coded as zero.

IV. Data

We use data from four major sources. The Windhover Database of Strategic Alliances contains information on pharmaceutical and biotechnology deals. It records information on all strategic alliance deals signed by biotechnology and pharmaceutical companies between 1991 and 2000, to the extent that information is publicly available. The dependent variable in our analysis of deal payments is defined as the total potential precommercial payments from the licensor (biotech firm) to the

15. In the regression, we omit the codevelopment indicator and include the three firm-size indicators and the interactions of the codevelopment indicator and the three firm-size indicators.

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licensee (pharmaceutical firm).[16] *Potential* refers to the scenario where all scientific milestones are achieved. As mentioned in the previous section, this measure of the deal price overstates expected precommercial payments because it assumes contingent milestone and sponsored research payments are paid with certainty. Furthermore, equity investments by the licensee are included in the deal price, although one could argue that the licensor gives up an equally valued asset in return, ownership in its firm. On the other hand, our measure of deal price underestimates the expected postcommercial payments to the selling firm because royalty payments are excluded.

Since the Windhover database includes all types of alliances but our theory applies to codevelopment deals, we apply a set of criteria to select single-product deals with an R&D component. Specifically, we exclude comarketing deals that are signed after a compound has been developed, transactions that involve multiple products or acquisitions of research divisions or entire companies,[17] and deals for platform technologies that may produce multiple compounds (e.g., access to a genomics database). These criteria yield 539 deals that have nonmissing values for the precommercial deal price as well as the other independent variables.

Windhover classifies each firm into a specific industry group (e.g., gene therapy, pharmaceutical, in-vitro diagnostics) according to its principal type of product. We create a biologic indicator variable that takes on the value of 1 for drugs developed by firms that focus on large molecules or antibodies.[18] Deal prices for biologics could be relatively low, all else equal, since biologics are generally more expensive to manufacture than chemical compounds and pharmaceutical firms are less likely to have a comparative advantage relative to biotech firms with biologics than chemical compounds. On the other hand, deal prices for biologics could be relatively high because biologics tend to have higher prices and are less likely to face generic competition than chemical compounds.[19] Finally, we create a set of 19 indicator variables for the therapeutic category of the

16. This figure includes upfront payments, sponsored research payments (usually a fixed amount per Ph.D. scientist assigned to perform research on the drug in question), investments in the licensor firm's equity, and potential milestone payments if designated events are achieved (e.g., initial phase 3 trial). Post-commercial royalty payments that the licensee may receive once the drug actually reaches the market are not included in the pre-commercial deal price.

17. Discovery-stage deals often involve a family of compounds where there is a single lead product. We include these deals in the analytic sample.

18. We considered two alternative definitions of a *biologic:* (1) drugs developed by companies that Windhover classifies as being "biotech" firms (87% of the deals in our sample) and (2) drugs developed by firms that focus on large molecules, antibodies, gene therapy, cell therapy, carbohydrates, genomics, liposomes, nonotechnology, gene transcription, or synthesis technologies (53% of the deals in our sample). We believe these alternative measures overstate the number of biologics in the sample.

19. There are no generic biologics in the United States, but some biologics (e.g., insulin) are facing generic competition in Europe and other countries.

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TABLE 1 Sample Means and Standard Deviations (n = 539)

Variable	Mean	Standard Deviation
Precommercial value of the deal ($ millions)[a]	29.300	37.100
Development stage of compound at time of deal:		
Preclinical	.616	.487
Phase 1	.079	.270
Phase 2	.121	.327
Phase 3	.147	.354
First deal for seller	.610	.488
Second deal for seller	.180	.384
First deal for seller signed after preclinical phase	.202	.402
Seller retains rights to		
U.S. market	.252	.434
Japanese market	.270	.444
Deal includes an equity investment	.472	.500
Reverse licensing deal	.026	.158
Log(public and private equity raised by biotech companies) in year prior to deal, $ millions	4.680	.645
Seller's enterprise value (market value of equity + book value of debt) in year prior to deal, $ millions[b]	2,216	11,527
Seller's enterprise value is missing	.333	.413
Buyer's enterprise value in year prior to deal, $ millions[c]	10,782	21,982
Buyer's enterprise value is missing	.218	.470

[a] Precommercial deal value is the sum of the up-front payments, sponsored research payments (usually an amount per scientist assigned to the compound), milestone payments, and equity investments.
[b] The mean presented for the seller's enterprise value is for the subset of 360 publicly traded firms whose financial data are recorded by Compustat.
[c] The mean presented for the buyer's enterprise value is for the subset of 421 publicly traded firms whose financial data are recorded by Compustat.

drug compound (e.g., gastrointestinal drugs), based on Windhover's modification of the World Health Organization (WHO) codes.

Sample means and standard deviations are reported in table 1. The mean precommercial deal value is $29.3 million in 1996 dollars, with a maximum deal value in our data set of $457 million. The standard deviation of deal price is larger than the mean, which indicates there is considerable variation and right skewness in the deal price distribution. The majority of deals are signed when the compound is still in the preclinical stage (which includes the discovery stage for this analysis), and in 95% of deals, the licensor is a biotech company. The majority of deals were also the first ever for the biotech companies, which is not surprising because many biotech companies were founded in the 1980s and went public in the late 1980s and early 1990s.

We report mean deal values by development stage in table 2. Deal prices increase monotonically by stage; firms out-licensing drug compounds in phase 1, phase 2, and phase 3 receive deal prices slightly larger than in early-stage deals. Since this total precommercial payment measure is not adjusted for risk or the time value of money, this trend by deal phase suggests that later-stage deals involve either greater retention of responsibilities for the seller or greater seller bargaining power.

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TABLE 2 Number of Deals and Deal Payments by Development Stage

	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

Source: Windhover Database.

We use Adis International R&D Insight Database to analyze the performance of drugs in clinical trials. Adis collects information on all drugs under active development by the international pharmaceutical and biotech industries, including the compound's generic name, company name, current development stage and development history, a description of adverse events and clinical trials, World Health Organization therapeutic indication categories (e.g., nervous system drugs), and launch dates by country for approved drugs.

Financial information on public biotech and pharmaceutical companies is available from Compustat. We collected information on the enterprise value of the buying and selling companies in the year prior to the deal. For companies that were private at the time of the deal but have since gone public, we used the Recombinant Capital RDNA database to obtain the postmoney value of company at the round of venture capital financing immediately prior to the deal in question. Since biotech firms carry little debt, the postmoney value of private companies should be analogous to the enterprise value of public biotech companies. In our sample, buyer firms are about five times larger than sellers on average, as measured by market capitalization. The total amount of public and private equity capital that biotech firms raised for each year between 1988 and 2000 was obtained from several sources.

Recombinant Capital recorded the financing history of over 550 biotech firms from the time of their first venture capital investment through their IPO, if it had occurred by July 2001. This information is from Securities and Exchange Commission (SEC) filings when the company goes public or acquires another firm. Our sample, therefore, does not include biotech firms that went out of business before going public or being acquired.

V. Results

A. Determinants of Deal Values

In table 3, we report coefficient estimates of the determinants of deal prices. The dependent variable is the logarithm of the total potential precommercial payments from the buyer-pharmaceutical firm to the seller-biotech, measured in thousands of 1996 dollars. In the first specification, we include drug characteristics only (indicator variables for therapeutic

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TABLE 3 Coefficient Estimates on the Determinants of Deal Values

Variable	Coefficient	SE	Coefficient	SE	Coefficient	SE
Stage of drug at time of deal:						
Phase 1	−.053	.238	−.095	.236	.344	.288
Phase 2	.601**	.208	.549**	.206	.941**	.254
Phase 3	.388**	.189	.372**	.187	.783**	.244
Seller maintains rights to						
U.S. market	−.306*	.182	−.293	.180	−.275	.179
Japanese market	−.211	.179	−.174	.177	−.179	.176
Biologic	−.311**	.155	−.356**	.154	−.368**	.153
Biotech equity raised, $t - 1$			.017	.099	.030	.098
First deal for seller			−.631**	.160	−.366*	.188
Second deal for seller			−.334*	.202	−.310	.201
First deal for seller and deal signed in phase 1, phase 2, or phase 3					−.701**	0.268
Constant	9.51**	.211	9.91**	.556	9.68**	.560
N	539		539		539	
R^2	.07		.150		.170	

NOTES.—The dependent variable is log (precommercial deal value in $000s), which includes up-front payments, sponsored research payments (usually an amount per scientist assigned to the compound), milestone payments, and equity investments. Nineteen indicator variables are included for the therapeutic category of the compound, using codes that Windhover adapted from the World Health Organization codes. We omit the indicator variable for deals signed when the compound was in the discovery or preclinical stage of development. Indicator variables are also included for deals that included an equity investment and for reverse licensing deals (except in column 1).

** Significantly different from 0 at the 5% level; * significantly different from 0 at the 10% level.

category and indicator variables for the compound's development stage). Of the 19 coefficients on the therapeutic category indicator variables (gastrointestinal, dermatology, and dental), 3 are significantly lower at the 10% level than for other compounds (coefficients not shown in table 3). Compounds can be assigned to multiple therapeutic categories, so there is no single omitted category. When the selling firm retains the right to develop and sell the drug in the United States, it receives a 26% lower price ($\exp(-0.306) - 1$) than if it grants the buyer worldwide rights. This is slightly lower than the U.S. share of total world pharmaceutical sales, which is around 40%. Deal payments for biologics are 27% lower than for nonbiologics, which is consistent with the perception that the manufacturing process for biologics is relatively complex and expensive or pharmaceutical firms have relatively little experience developing biologics and therefore add relatively little value to such an alliance. The coefficients on the phase-2 and phase-3 indicator variables are positive and significant.

In the second specification of table 3, we add information on the deal structure (e.g., whether the deal included an investment by the buyer in the selling firm's equity), the experience of the selling firm, and the opportunity cost of alternative financing, measured by total biotech equity financing in the year preceding the deal. We include two variables to measure the seller's experience: an indicator that equals 1 if this is the firm's first deal and an indicator that equals 1 if this is the firm's second

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deal (two or more prior deals is the omitted variable). Firms negotiating their first deal receive payments that are 47% lower ($26.9 million), on average, than firms with at least two prior deals.[20] This discount for inexperience declines to 28% ($16.3 million) for the second deal.[21] The coefficient on the first-deal variable is significantly different from zero at the 1% level, whereas the coefficient on the second deal variable is significantly different from zero at the 10% level. These results suggest that pharmaceutical firms incur substantial search costs. As shown later, the value of the signal to biotech firms ($19.5 million in the first-difference specification of table 6) is substantial, although smaller than the implicit payment these firms make for producing the information.

An alternative explanation for the negative coefficients on the first- and second-deal variables is that, as biotech firms learn, the incremental value of codeveloping a drug with a pharmaceutical firm decreases. If pharmaceutical firms capture these synergies due to negotiating power, then deal payments are relatively small for inexperienced biotech firms. The two explanations need not be mutually exclusive; deal payments might increase with the seller's experience due to both learning and signaling. We need more specific data on the rights and responsibilities of the companies involved in the alliances to separately measure these two effects.

Prices for phase-2 and phase-3 deals are 73% and 45% higher, respectively, than for deals where the compound is in the discovery or preclinical stage (the omitted category), controlling for drug and deal characteristics. Since we expect total potential precommercial payments to be invariant by stage of deal, the increase in deal prices for phase-2 and phase-3 deals is consistent with biotech firms taking on greater responsibilities in later-stage deals (and, therefore, being reimbursed at a higher rate from the buyer), higher unobserved quality of late-stage products, or greater bargaining power by biotech companies on later-stage drugs due to a relatively small number of sellers. The coefficient on the index of biotech funds raised from the equity markets is insignificant.

In the third column of table 3, we include an indicator variable if the selling firm is signing its first deal and the deal is signed in a clinical phase (phase 1, phase 2, or phase 3). The coefficient on this variable is negative and large, and the coefficients on the phase-1, phase-2, and phase-3 development-stage indicators are larger than before. A biotech firm signing its first deal in the discovery or preclinical phase receives payments

20. Since the dependent variable has been logarithmically transformed, to estimate the magnitude of the first-deal discount in dollars, we use the regression coefficients from table 3 to calculate $\exp(\gamma\mathbf{X} + 0.5\sigma_{\varepsilon}^2)$, separately for companies that are signing their first deal and those that have already signed at least two deals (Manning 1998). The term σ_{ε}^2 refers to the estimated ordinary least squares residual variance.

21. We also tried a specification including indicator variables for three and four prior deals, but these coefficients were insignificant.

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TABLE 4 Coefficient Estimates on the Determinants of Deal Values

	Coefficient	Standard Error
Stage of drug at time of deal:		
Phase 1	−.12	.23
Phase 2	.454**	.20
Phase 3	.346*	.19
Seller maintains rights to		
U.S. market	−.21	.18
Japanese market	−.11	.17
First deal for seller	−.571**	.16
Second deal for seller	−.25	.20
Biotech equity raised, $t - 1$	.04	.10
Seller's enterprise value, $t - 1$	.01	.01
Indicator if missing enterprise value for seller	.16	.14
Buyer's enterprise value, $t - 1$	.0178**	.00
Indicator if missing enterprise value for buyer	.380**	.13
Constant	9.13**	.56
N	539	
R^2	.21	

NOTES.—The dependent variable is log(precommercial deal value in $000s). Nineteen indicator variables are included for the therapeutic category of the compound, using codes Windhover adapted from the World Health Organization) codes. We omit the indicator variable for deals signed when the compound was in the discovery or preclinical stage of development. Indicator variables are also included for deals that include an equity investment and for reverse licensing deals. Buyer and seller enterprise values are measured in $ billions.

** Significantly different from 0 at the 5% level; * significantly different from 0 at the 10% level.

that are an estimated $13.2 million lower than a firm that has already signed at least two deals. By contrast, a biotech signing its first deal in a clinical stage experiences a much larger discount of $39.7 million relative to an experienced biotech firm.

These results are consistent with scenarios 2 and 3 of the signaling model, where biotech firms with low-quality products cannot afford to reimburse a pharmaceutical firm for information costs until the later development stages, when the costs are relatively low. The small deal payments to inexperienced firms for phase-1, phase-2, and phase-3 drugs, relative to firms that have already signed alliances, reflects the low quality of the drugs. This poor quality is unobserved to us but inferred by prospective buyers, because the biotech firm was unable to sign a deal earlier in the drug's development.

In table 4, we add firm-specific financial information on the sellers and buyers to further examine whether liquidity constraints or bargaining power affects deal payments. The coefficient on the seller's enterprise value is positive, as expected, but not significant. The coefficient on the indicator variable for selling firms with missing financial information, which are predominantly private biotech companies and small public biotechs, is also insignificant. The coefficient on the equity index is positive but insignificant, as before. Thus, we find little evidence that the status of the equity markets affects deal payments, even for small

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biotechs that are more likely to be cash constrained. Combining these results with those from Lerner and Tsai (2000), this suggests that liquidity constraints lead to adjustment in rights transferred rather than in the price paid for those rights, contrary to what might be expected under the efficient-markets hypothesis.

The coefficient on the buying firm's enterprise value is positive and significant, implying that large pharmaceutical firms pay more to in-license compounds than small firms. A $1 billion increase in a buyer's market capitalization is associated with a 1.8% increase in the deal payment. This result is consistent with the presence of economies of scale and scope in R&D that allow larger pharmaceutical firms to outbid smaller firms when in-licensing compounds. It may also reflect unobserved quality, if larger firms bid only for those products that have relatively large expected revenues. In this specification, deal payments for phase-2 drugs were 45% larger than for preclinical drugs. As before, we interpret this increased payment as evidence that the selling firm takes greater responsibility in the subsequent development of the drug.

B. Effect of Deals on the Valuation of Firms

If alliances with pharmaceutical firms allow private biotech firms to signal the quality of the firm's product pipeline and management to venture capitalists, then alliances are predicted to cause an increase in the market value of a firm. We present some descriptive data in table 5 on the venture capital financing history and initial public offerings of 566 biotech firms. Biotech firms typically raise several rounds of private equity before going public or being acquired. As displayed in the final column of table 5, 58% of the biotech firms raised between three and five rounds of private equity.

The mean market value of a biotech firm after its first round of venture capital financing was $11.1 million, and the value more than doubled by the second financing round (second column of table 5). Values continue

TABLE 5 Alliance Activity and Private and Public Market Valuation of Biotech Firms (n = 566)

Financing Round	Biotech Firms That Signed a Deal before the Round	Mean Valuation after Financing ($millions)	Biotech Firms for Whom This Is the Final Venture Capital Round
1	1.2%	$11.1	11.7%
2	3.2%	$26.3	14.6%
3	5.1%	$42.7	21.2%
4	7.8%	$55.3	20.3%
5	10.7%	$68.0	17.3%
6	11.8%	$84.3	7.3%
7–9	12.3%	$120.2	7.7%
Initial public offering	15.70%	$162.2	

Source: Recombinant Capital.

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TABLE 6 Impact of Deals on Biotech Venture Capital and Initial Public Offering Valuations

Dependent variable	Log(Company Value$_n$) After Financing Round n	Log(Value$_n$) − Log(Value$_{n-1}$)
Biotech had signed 1 deal prior to financing round n	.380** (.0720)	
Biotech had signed 2 or more deals prior to financing round n	.392** (.1680)	
Biotech signed its first deal between round $n - 1$ and round n		.232** (.0817)
Biotech signed a deal between round $n - 1$ and round n, and it was not its first deal		.1070 (.1240)
Second venture capital round	.963** (.0420)	
Third venture capital round	1.51** (.0550)	−.404** (.0480)
Fourth venture capital round	1.76** (.0670)	−.609** (.0550)
Fifth–ninth venture capital round	2.04** (.0820)	−.746** (.0490)
Initial public offering	2.59** (.0640)	−.211** (.0540)
Months between financing rounds		.0011 (.0014)
Constant	1.76** (.0770)	0.984** (.0600)
Observations	2,477	1,883
R^2	.59	.17

NOTE.—The dependent variable in the first specification is the logarithm of a company's postmoney valuation after a round of venture capital financing or in an initial public offering, measured in millions of dollars. The dependent variable in the second specification is the difference in the logarithm of the company's postmoney valuation between subsequent rounds of venture capital financing or between the final venture capital round and the IPO, also measured in millions of dollars. We include a set of indicators for the year of the financing and the financing round (the first venture capital round is omitted in the first specification, and the change in value between the first and second venture capital rounds is omitted in the second specification). We adjust the standard errors to allow error terms to be correlated within a firm over financing rounds.

** Significantly different from 0 at the 5% level; * significantly different from 0 at the 10% level.

to grow between venture capital rounds, although at decreasing rates in percentage terms. Three-quarters of these 566 firms had gone public by 2001. As reported in the first column of table 5, few biotech firms had signed any deals prior to their first financing round. By the time of the IPO, about one-sixth of the biotech firms had formed at least one alliance. If deals function as quality signals, therefore, they are probably not the only signaling mechanism. Of the 90 firms that signed a deal prior to their IPO, 82% signed one deal only, 10% signed two deals, and only 8% signed three or more deals.

We present the valuation regression results in table 6. In the first specification, the dependent variable is the logarithm of the firm's value at the conclusion of a financing round, measured in millions of dollars.[22] Valuations at each venture capital round and the IPO, if it occurred, are pooled together. We adjust the standard errors to allow the error terms to be correlated within a firm across the different financing rounds.[23]

22. Deal prices are converted to 1996 dollars using the producer price index.

23. Bertrand, Duflo, and Mullainathan (2002) show that failing to correct for serial correlation in the error terms can bias downward the standard errors when difference-in-difference

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Biotech firms that signed a single deal received valuations that were 46.2% higher, and biotech firms that signed two or more deals received valuations that were 48.0% higher, on average, than firms that had not yet signed a deal (the omitted variable). Based on these results, the estimated valuation premium associated with signing a deal is $20.2 million.[24] We cannot reject the hypothesis that the coefficients on the one-deal and two-plus-deal coefficients are equal, which suggests that one deal is sufficient to signal a biotech firm's quality. With symmetric information, a biotech company's second deal should not affect its value because the deal payment is commensurate with the value of the assets exchanged.

The coefficient on the second venture capital round variable indicates that the value of biotech firms at the end of the second financing round are 162% higher than in the first round (the omitted round), on average. Values increase monotonically over the subsequent private equity rounds and the IPO. We control for the year of financing but do not report the coefficients in table 6. Market values increased substantially in the late 1990s and in 2000. Relative to 1991, biotech valuations were 35% higher in real terms in 1997, 51% higher in 1998, 109% higher in 1999, and 224% higher in 2000.

The second column of table 6 presents results of the first-difference valuation regression (as described by equation [5]). Time-invariant characteristics that are correlated with a firm's value drop out of the first-difference specification, so we should obtain a more precise measure of the incremental signal value of a deal. A biotech firm signing its first deal experiences an estimated 26.2% increase in value, on average, at its subsequent financing round relative to biotech firms that did not sign a deal in the interim. This result increases our confidence that the step-up in a biotech firm's market value can be attributed to the relatively recent deal signing. The coefficient from the first-difference specification is smaller than the estimated impact of deals from the cross-section regression but still significantly different from zero and economically meaningful. Based on the preferred estimate from the first-difference specification and the sample mean biotech valuation ($74.4 million), a biotech firm receives an estimated $19.5 million higher valuation due to the alliance's signal. The coefficient on a deal other than the biotech firm's first deal is positive but insignificant, which is consistent with the cross-section regression where the coefficients on the first-deal and two-plus-deal variables are essentially the same. This implies that it takes only one deal to signal a biotech firm's quality to private investors. Only 16 deals in our

models are estimated with ordinary least squares. These authors also show that our method of adjusting the standard errors generally removes most of the bias when the number of groups is large, as is the case with our 562 firms. Hausman and Kuersteiner (2003) show that, under certain circumstances, feasible generalized least squares are more efficient than ordinary least squares.

24. This estimate is for a third round of venture capital financing that occurred in 1991.

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data are by firms that have already signed a deal, so the lack of significance may be due to a small sample.

These results are consistent with scenarios 2 and 3 of our model, where pharmaceutical firms sign codevelopment deals with high-quality biotech firms only. The signal from the deal allows high-quality and low-quality firms to be valued appropriately by venture capitalists. The $19.5 million premium associated with a deal measures the difference in the value of a high- and low-quality firm $(V_H^F - V_L^F)$, once investors can distinguish the two quality types. We cannot rule out scenario 1, however, where all biotech companies sign deals and venture capitalists infer the quality of firms from the magnitude of the deal payments. In this latter scenario, the coefficient on the deal variables in table 6 indicate that more high- than low-quality firms sign deals, or the magnitude of the undervaluation in the previous pooling equilibrium exceeds the magnitude of the overvaluation.

The results from the valuation analysis suggest that gains from trade in codevelopment is not the sole rationale for deals. If it were, and if venture capitalists anticipated that firms would enter into deals when deals are efficient, the realization of such alliances would have no effect on firm valuations. Our valuation analysis focuses on private biotech firms because that is where we think information asymmetry problems might be particularly acute.

C. Postdeal Performance

If biotech firms exploit their informational advantage to out-license low-quality drugs, then drugs that are codeveloped should be less likely to advance (Pisano 1997). This possible information asymmetry is an alternative explanation for our finding that biotechs receive discounted payments on their first deal. Conversely, if pharmaceutical firms can distinguish high- and low-quality drugs, then drugs that are codeveloped should be just as likely to advance as those developed independently. Finally, if there are benefits of codevelopment (the gains-from-trade model) or if only high-quality drugs are out-licensed (scenarios 2 and 3 of the signaling model), then drugs that are codeveloped should be more likely to advance than those developed independently.

In table 7, we present selected coefficient estimates from three different logit regressions using the Adis database of drugs under development. The first regression includes all drugs that began a phase 1 trial. Each observation is a condition for which a drug is being tested, so there may be multiple observations for a particular drug. The dependent variable takes the value 1 if phase 1 is completed and a phase-2 trial is initiated for the condition in question, and 0 otherwise. To control for firm experience, we include separate indicator variables for companies that originated three or fewer drugs during the sample period (1991–2000),

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TABLE 7 Logit Coefficient Estimates for the Determinants of R&D Success

Sample	Dependent Variable: 1 if Completed Phase		
	Drugs That Started Phase 1	Drugs That Started Phase 2	Drugs That Started Phase 3
Small company is originator (omitted group: nonindustrialized source):			
Developed independently	.221 (.251)	−.371 (.230)	−1.52** (.311)
Codeveloped	.466* (.264)	.734** (.217)	1.34** (.294)
Medium-sized company is originator:			
Developed independently	−.323 (.230)	−.724** (.220)	−1.01** (.277)
Codeveloped	1.22** (0.257)	1.35** (.209)	1.19** (.245)
Large company is originator:			
Developed independently	−.551** (.223)	−.513** (.203)	−.505* (.259)
Codeveloped	1.13** (.244)	.832** (.189)	0.666** (0.223)
Constant	1.13** (.220)	.529** (.184)	0.697** (.218)
Psuedo-R^2	.08	.09	.14
N	2,392	1,579	1,083
Marginal effect of codevelopment on probability of advancing for a			
Small firm	.041	.171	.302
Medium-sized firm	.125	.310	.288

NOTE.—Observations are specific conditions for which a drug is being developed to treat. Dependent variable is 1 if a drug advanced to the subsequent development stage or was approved by the FDA. The logit regressions include 13 indicators for the therapeutic category of the compound. Standard errors are in parentheses. To address right censoring, we calculate the maximum length of time it took for a drug to complete each development stage (5 years for phase 1, 5 years for phase 2, and 4 years for phase 3). Drugs that were censored and had started a stage within these time periods were omitted from the regressions; drugs that were censored and had started a stage beyond these time periods were assumed to have failed. Small companies originated 3 or fewer drugs during our sample period (1991–2000); medium-sized companies originated between 4 and 24 drugs; and large companies originated 25 or more drugs.

* Significantly different from 0 at the 10% level; ** significantly different from 0 at the 5% level.

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between 4 and 24 drugs, and 25 or more drugs.[25] Biotech firms are in the small- or medium-sized category whereas most pharmaceutical firms are in the largest category. Drugs that were originated by a nonindustrialized source, which is usually a university, are the omitted group. We interact the three indicator variables for firm experience with an indicator variable if the drug is being codeveloped. Recall that a majority of deals in our data set (61%) represent the first deal signed by a biotech company, so most of the alliances involve inexperienced biotech firms.

In the first column, the three coefficients on the codevelopment interaction variables are positive and significant; compounds being developed through an alliance are more likely to complete phase-1 trials than compounds developed independently by small, medium, or large firms. These coefficients are also economically meaningful. A drug originated by a medium-sized firm that is codeveloped has a probability of completing a phase-1 trial that is an estimated 12.5 percentage points higher than an otherwise similar drug developed independently (marginal effects of codevelopment are reported in the bottom rows of table 7). Thus contrary to Pisano (1997), we find no evidence that biotech firms use their informational advantage to out-license relatively unattractive compounds. Our results are consistent with a situation where low-quality drugs are less likely to be out-licensed because their parent firms cannot reimburse pharmaceutical firms for the information costs (scenarios 2 and 3 of the signaling model) or the collaboration improves the likelihood a drug will advance.

The last two columns of table 7 report similar logit regressions for drugs that began phase-2 and phase-3 clinical trials. The dependent variable in each specification is 1 if the drug successfully completed that single stage. As before, the coefficients on the codevelopment interactions are positive and significant. The predicted probability that a drug originated by a small firm and developed jointly with another company will complete phase-2 and phase-3 trials is 17 and 30 percentage points higher, respectively, than a drug the firm originates and develops independently. We find no evidence, therefore, that the lower payments accepted by inexperienced biotech companies are due to the greater scientific risk of the product.

VI. Conclusions

The analysis in this paper sheds light on several hypotheses regarding the effects of buyer and seller characteristics, liquidity constraints, and asymmetric information in the market for biotech-pharmaceutical deals.

25. The experience thresholds we use to define small, medium, and large firms are arbitrary but they do divide the sample of compounds into three approximately equal-sized groups. The results are qualitatively similar if we define small, medium, and large firms as those that have originated 5 or fewer drugs, between 6 and 29 drugs, and 30 or more drugs, respectively.

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We find that biotechnology companies receive a 47% discount for their first deal and a 28% discount for their second deal and that these discounts are not consistent with the drugs' postdeal performance. These discounts are consistent with a model where deals signal the selling firm's asset and managerial quality to equity markets. Pharmaceutical companies are plausibly better able to evaluate biotech companies than pure financial intermediaries. The discounted payments accepted by inexperienced biotech firms represent implicit payments to reimburse the pharmaceutical company for information costs. Since a pharmaceutical company takes not only an equity stake in a small firm but also acquires rights to the assets, the pharmaceutical firm may have stronger incentives to invest optimally in information gathering than a venture capitalist that takes only a partial and temporary equity share. The fact that drugs in biotech-pharmaceutical alliances perform better in subsequent trials than products developed solely in-house by biotech or pharmaceutical firms confirms that codevelopment adds sufficient value to outweigh any moral hazard problems that result from sharing development responsibilities. These findings are inconsistent with the lemons hypothesis, that biotech companies are able to out-license their least promising drugs. Our finding that the discount for first deals does not decline or disappear for later-stage drugs, when more objective information is available, provides further evidence against the lemons hypothesis.

Although biotech companies take a substantial discount on their first deal, this nevertheless appears to be rational, because a deal with a pharmaceutical company sends a positive signal to prospective investors. We find that biotech firms that have signed a deal receive substantially higher valuations from venture capitalists and other investors at subsequent financing rounds. The magnitude of this premium ($19.5 million in the preferred first-difference specification) offsets most of the discounted deal payments accepted by inexperienced biotech firms ($26.9 million). This evidence of positive effects of deals on subsequent financing is more consistent with the signaling model than with the simple gains-from-trade model. However, the fact that even established biotech firms continue to do deals suggests that deals can provide a means to take advantage of differing expertise to increase real productivity, as well as their information-producing, signaling function.

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