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Do equity financing cycles matter? evidence from biotechnology alliances[☆]

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Abstract

In periods characterized by diminished public market financing, small biotechnology firms appear to be more likely to fund R&D through alliances with major corporations rather than with internal funds (raised through the capital markets). We consider 200 alliance agreements entered into by biotechnology firms between 1980 and 1995. Agreements signed during periods of limited external equity financing are more likely to assign the bulk of the control to the larger corporate partner, and are significantly less successful than other alliances. These agreements are also

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disproportionately likely to be renegotiated if financial market conditions subsequently improve.

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1. Introduction

The clustering of equity offerings in “hot issue” markets has been documented in the academic literature since [Hickman \(1953\)](#). Theoreticians have suggested that external financing is an important driver of organizational structure and managerial behavior. Yet the implications of variations in equity financing activity for the allocation of resources to firms and their subsequent performance have been little explored empirically. This paper takes an initial step towards understanding how changes in financing availability affect organizational structure and outcomes. Rather than studying the impact of financing conditions in a variety of industries, however, we examine a single arena: technology alliances between small biotechnology firms and larger corporations.

While this approach restricts the generality of the results, it has three advantages:

- First, the theoretical literature makes specific predictions as to the effects of financing availability fluctuations on the biotechnology industry. [Aghion and Tirole \(1994\)](#) argue that in settings where the R&D firm does not have initial bargaining power, an ideal allocation of control rights might not occur. If it is desirable for control to be transferred to the R&D firm, the best outcome will not be achieved: the financing firm might be willing to transfer control, but the R&D firm will not have enough resources to compensate the financing firm. An inefficient allocation of the ownership and control results.
- Second, equity financing of biotechnology firms has undergone dramatic variations over the years. These shifts have been largely in the nature of industrywide shocks. In the years under study, relatively few biotechnology drugs had been approved. Unexpected events occurring at a single biotechnology firm—e.g., the rejection of a promising drug candidate—had dramatic effects, all firms’ abilities to raise equity.
- Finally, a great deal of information is available about biotechnology projects. The bio-engineered compounds that are the subject of the alliance agreements must undergo a rigorous and well-documented regulatory review process. Due to the importance of the alliance agreements as financing sources, almost all important biotechnology alliances are publicly filed. Other critical factors can also be identified and controlled for.

We first consider why increases in information asymmetries might lead young firms to increasingly rely on large corporations for financing. Large corporations could have the specialized knowledge and expertise to finance younger firms, even when information asymmetries deter public market investors from providing equity. This possibility is borne out in an analysis of the financing choices of a panel of 49 biotechnology firms. While the regressions in this section are statistically significant, their economic significance is less impressive.

We then consider the alliance agreements themselves. We show that in periods when public equity financing is readily available, the agreements are more likely to grant key control rights to the R&D firm. This pattern—consistent with theory—holds even after controlling for variations in the quality of the technology in the agreement.

We then examine whether the agreements are successful in terms of the progress of the product under development. Alliances that grant the bulk of the control to the R&D firm are more successful, an effect that is more pronounced in weak financing markets, as [Aghion and Tirole \(1994\)](#) predict.

We finally examine the likelihood of renegotiation. If it would have maximized innovative output to assign control to the small biotechnology company, but this allocation of control was precluded by financial market conditions, then we should see a distinct pattern in renegotiations. In particular, when financing conditions for biotechnology firms improve, the agreements that assign the bulk of the control to the financing firm should be disproportionately renegotiated. The empirical results are consistent with this pattern.

This paper is at the intersection of two bodies of literature. A substantial body of work examines the implications of financing availability: for instance, how financing constraints affect the investment policies of firms ([Hubbard, 1998](#)) and the relation between financial market development and aggregate economic growth ([Levine, 1997](#)). Similarly, organizational structure and its implications have been extensively scrutinized in the industrial organization literature (see, for instance, [Milgrom and Roberts, 1992](#)). [Bolton and Scharfstein \(1990\)](#) show that when young firms do not have “deep pockets”—in particular, when they rely on outside financiers for support as the firm evolves—concerns about predatory behavior by rivals may have a substantial impact. In particular, these worries lead financiers to lower the sensitivity of the refinancing decision to performance, thereby weakening managers’ incentives to succeed. Still, little empirical attention has been devoted to these issues.

This paper is also related to the literature on the variation in equity issuances over time, which emphasizes the importance of information asymmetries. [Mackie-Mason and Jeftrey \(1990\)](#) shows that information problems appear to influence publicly traded firms’ choices between private and public equity. Similarly, [Korajczyk et al. \(1991\)](#) demonstrate how the timing of earnings announcements affects when firms issue equity. [Bayless and Chaplinsky \(1996\)](#) show that the price reaction to equity issue announcements in periods of high equity issue volume is less negative on average than in periods of low equity issue volume, which they argue reflects reduced information asymmetries between issuers and investors. This paper suggests that these variations have real effects on firm performance.

The organization of the paper is as follows. Section 2 discusses the theoretical rationales for the empirical analysis. Section 3 provides a brief introduction to the role of R&D alliances in the biotechnology industry, and the evidence suggesting that there is a close mapping between the theoretical work and reality. Section 4 describes the data sets and the analyses are presented in Section 5. The final section concludes the paper.

2. Theoretical perspectives

2.1. The determinants of equity market cycles

Leland and Pyle (1977) and Myers and Majluf (1984) were among the first to suggest that information asymmetries can preclude firms from financing positive net present value projects. Even if the entrepreneur understands the value of the opportunity, the project will go unfinanced if he or she cannot convey this information to a potential financier. These information problems are most severe for firms in the early stages of development. In such settings, there is often little verifiable information. Even if audited financial statements are available, accounting data may not provide much information about an early stage firm.

In many studies of information and managerial decision-making, shifts in the information environment are presumed to be firm specific. But in industries with unproven prospects, changes in information asymmetries surrounding individual firms may be positively correlated. If many publicly traded companies have still not proven themselves to be profitable—such as was true in biotechnology in the 1980s and 1990s and electronic commerce in the 1990s—new information about one firm can change the evaluation of many similar firms. Similarly, economywide shocks can shift investors' evaluation of information problems surrounding a whole class of firms, or even firms in all industries (Bayless and Chaplinsky, 1996).¹

The role of intermediaries who finance young firms has been increasingly understood in light of these information problems. Financial economists emphasize the intensive *ex ante* due diligence and monitoring activities in connection with a financing provided by commercial banks (Diamond, 1991), private placement investors (Hertzel and Smith, 1993), or venture capitalists (Chan, 1983). These activities enable the investments to be made, even in settings with substantial information problems. Intermediaries provide other benefits as well. For instance, an intermediary such as a venture capitalist may have extensive experience in an industry, and can provide the firm's management with strategic guidance. Alternatively, the intermediary might own complementary assets (e.g., a production facility or a sales force in the case of a corporate partner) that make the young firm more effective.

¹Other factors may also affect the decision to issue equity. Many papers suggest that firms issue equity when they are overvalued (or expect to be overvalued): examples include Baker and Wurgler (2000), Lee et al. (1991), Lerner (1994), Lowry (2001), and Pagano et al. (1998). Many of these studies suggest that there is an industry component to this investor sentiment.

At the same time, these activities are not costless. The human capital required to assess and monitor investments is likely to take years to develop. The alliance agreements themselves are time-consuming and costly to negotiate and implement. As a result, the intermediaries require a return that compensates them for their investment of both financial and human capital. Once firms have resolved the initial information problems, they are likely to shift to public investors, who do not demand as great a premium. As the marginal benefits of obtaining external financing from knowledgeable intermediaries declines, the higher cost of their funds are likely to drive firms to the public markets. Because of the importance of complementary assets, however, we expect to see some alliances being formed even when public financial markets are readily accessible.

2.2. *The impact of public market shifts*

The literature review above suggests some reasons why the financing of firms by the public markets and informed private investors may shift over time. We now consider a theoretical depiction of how these shifts can affect one set of economic interactions: the relationship between small and large firms in strategic alliances.

Numerous models, beginning with [Grossman and Hart \(1986\)](#) and [Hart and Moore \(1988\)](#), consider incomplete contracting between a principal and an agent. A typical assumption is that it is impossible for the two parties to write a verifiable contract, enforceable in a court of law, that specifies the effort and final output of the two parties. This is because there are many possible contingencies, not all of which can be anticipated at the time the contract is drafted. Due to this nonverifiability problem, these models suggest that it is optimal for ownership of the project to be assigned to the party with the greatest marginal ability to affect the outcome. This party, who will retain the right to make the decisions that cannot be specified in the contract, should also receive any surplus that results from the project. Because of this incentive, the party will make the decisions that maximize—or come close to maximizing—the returns from the project.

[Aghion and Tirole \(1994\)](#) adapt this general model to an R&D alliance between two firms. In their basic model, the authors assume that the research unit is without financial resources of its own, cannot borrow any funds, and has no ability to commercialize the innovation itself. As a result, it turns for financing to a customer, a firm that may intend to use the product itself or to resell it to others but cannot make the discovery independently. The success of the research project is an increasing function, though at a decelerating rate, of both the effort provided by the research unit and the resources provided by the customer.

Developing a contract between the two parties is challenging. While the ownership of the product can be specified in an enforceable contract, and the resources provided by the customer can also be so specified, uncertainty precludes writing a contract for the delivery of a specific innovation. Similarly, an enforceable contract cannot be written that specifies the level of effort that the research unit will provide.

[Aghion and Tirole \(1994\)](#) consider two polar cases: when the research unit has the *ex ante* bargaining power, and when the customer does. When the research unit has

the bargaining power, the ownership of the research output will be efficiently allocated. If the marginal impact of the research unit's effort on the innovative output is greater than the marginal impact of the customer's investment, then the research unit will receive the property rights. If not, the research unit will transfer ownership to the customer in exchange for a cash payment. This result is similar to that of [Grossman and Hart \(1986\)](#).

When the customer has the bargaining power, however, a different pattern emerges. If it is optimal for the customer to own the project, it will retain the project. If, however, it would maximize innovation for the property rights to be transferred to the research unit, the ideal outcome will not be achieved. The customer will be willing to transfer ownership, but the cash-constrained research unit will not have enough resources to compensate the customer. As a result, an inefficient allocation of the property rights occurs, with the customer retaining the rights to the invention.

While [Aghion and Tirole \(1994\)](#) do not explicitly depict a role for the public market, it is reasonable to believe that variations in the availability of public financing will affect the bargaining power of R&D firms. During periods when public financial markets are readily accessible, these firms may be able to finance projects through either public equity issues or alliances. But during periods when equity issues are more difficult, R&D firms may have few alternatives to undertaking alliances. In the latter periods, it is also reasonable to assume that the R&D firm's bargaining power will be considerably reduced.

The claim that control rights are more likely to be transferred to the financing firm during periods of diminished public equity market activity is also supported by related models. [Holmstrom and Tirole \(1997\)](#) depict a setting where an economic shock affects the disbursement of capital by both public investors and intermediaries. Transposed to our setting, after a negative shock in the public equity market, the share of projects that can be directly financed through public investors will fall. More firms—particularly those with the greatest need for capital—will turn to intermediaries that can provide intensive oversight along with the needed capital, or else not be financed at all. In these cases, the intermediaries will insist on more stringent conditions in exchange for their capital. [Aghion and Bolton \(1992\)](#) show that when entrepreneurs have insufficient income to pledge to investors, they may only be able to raise financing by giving investors a control right (e.g., the right to terminate a project). While it can reduce the net present value of the project (the action may be sufficiently painful to the firm's employees and managers that social welfare is harmed, even if the firm's profits are enhanced), the transfer of control insures that the investors will receive sufficient proceeds to compensate them for their investment. Firms with financing problems may consequentially grant "excessive" (at least relative to the unattainable, first-best outcome) control rights to investors. These two papers also suggest there will be a strong linkage between the transfer of control and the public equity market conditions.

One way to visualize this prediction is shown in [Fig. 1](#). The curved line depicts the value of a project that would ideally be largely in the control of the R&D firm. In periods with strong financing markets, the two parties can reach any possible contract, and will assign a large fraction of the control of the project to the R&D

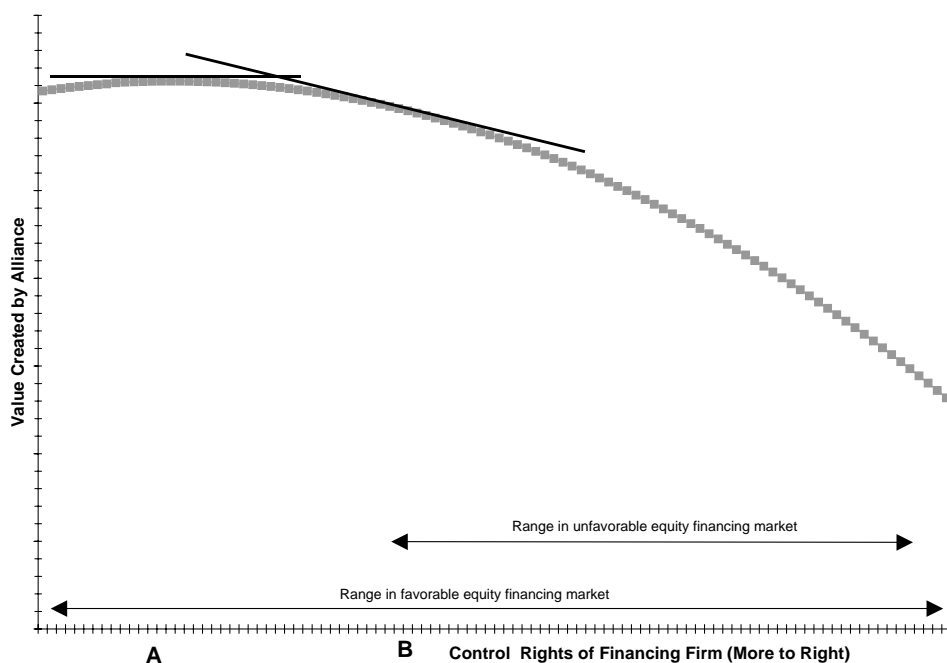


Fig. 1. Illustration of predicted marginal impact of a shift in the allocation of control rights on the alliance outcome when equity financial markets are favorable and unfavorable (which affects the range of contracts that the two parties can reach).

firm (Point A). A weak financing market, however, limits the set of contracts that the two parties can arrive at. As discussed above, they may negotiate a contract that does not maximize the value of the project (Point B). Fig. 1 treats control as a continuous variable, rather than as an indivisible right. It is unlikely that all control rights will be allocated to the R&D firm in any alliance, since in many areas (e.g., marketing) the financing firm will be far more informed.

The model suggests that the marginal impact of providing an additional control right to the financing firm will be quite different in the two markets. In a strong financing market, since the control rights are allocated in a way that maximizes value, the addition of a single control right is unlikely to have much impact. In a weak financing market, however, the shift may lead to a substantial decrease in value.

3. The biotechnology industry as a testing ground

The biotechnology industry originated in the mid-1970s. The many new firms that were formed in the subsequent decades sought to commercialize scientific developments in genetic engineering. To this day, the industry remains characterized by numerous small research-intensive firms, who finance themselves primarily through public equity issues and alliances with pharmaceutical companies.

A natural question is the extent to which the theoretical depictions correspond to the reality of the biotechnology industry. Lerner and Merces (1998) describe three case studies of alliances between biotechnology and pharmaceutical firms. These studies highlight three ways in which biotechnology alliances resemble the theory:

- First, the biotechnology industry is characterized by considerable information asymmetries. Biotechnology-based products frequently take between one and two decades and many hundreds of millions of dollars to develop. It is frequently difficult for investors to assess how the firm is progressing.
- Second, information problems appear to be correlated across firms. Because there are so many ambiguities surrounding biotechnology R&D, surprises affecting one firm can lead investors to reassess their beliefs about the viability of biotechnology research and/or the industry's commercial prospects. For instance, the announcement in January 1993 by Centocor that clinical trials of its flagship Centoxin product were being terminated led to dramatic declines in both the share prices and the equity financing activity of most biotechnology concerns. (Worries about the implications of the Clinton health care plan also had a depressing effect on activity in the 1992–1994 period.) As a result, the amount of capital raised from the public markets has been highly variable (see Fig. 2).

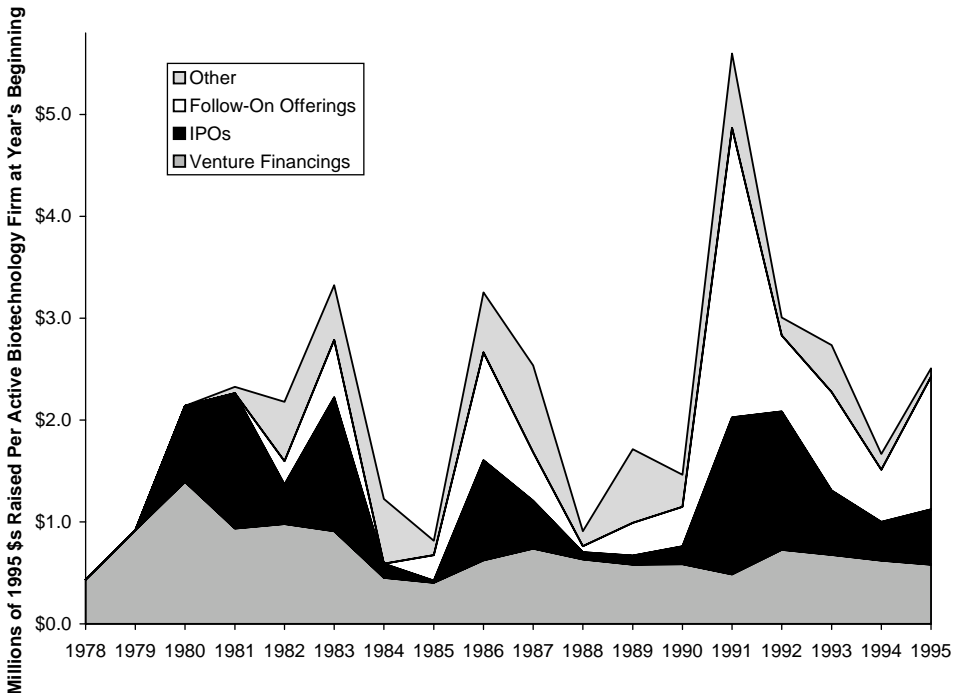


Fig. 2. External financing of the US biotechnology industry. The chart depicts the amount raised by US new biotechnology firms through private venture financings, initial public offerings, follow-on public equity offerings, and other sources. (Alliance-related financings are excluded.) Amounts are normalized by the number of firms active in the industry at the beginning of each year.

- Finally, in addition to information asymmetries, there is also a great deal of uncertainty in biotechnology research. This makes it difficult for contracting parties to specify the features of the product to be developed. Similarly, the complexity and unpredictability of biotechnology research present challenges in drafting an enforceable agreement that specifies the contributions of the R&D firm. In particular, firms that contract to perform R&D in alliances frequently have ongoing research projects of their own, in addition to the contracted efforts. In case of a dispute, it may be very difficult for the financing firm to prove that the R&D firm has employed alliance resources to advance its own projects.

At the same time, the case studies reveal that biotechnology alliances present a more complex picture than many incomplete contracting models. First, the basic Aghion-Tirole model presents a setting where the parties bargain over a single, indivisible ownership right.² By way of contrast, actual alliances are complex documents, often extending for 100 pages or more and assigning a wide variety of control rights.

Nonetheless, conversations with practitioners identified five control rights as key to the management of most, though not all, alliances. They are as follows:

1. *Management of clinical trials.* Not only are applications for regulatory approval of human and agricultural bio-engineered products protracted and costly, they also involve many decision points. For instance, while a human therapeutic product may have diverse potential uses, regulatory approval is given only for specific uses. Thus, the financing firm may not wish to apply for approval of a therapeutic treatment for a disease for which it has an existing product, lest it cannibalize existing sales, even if its R&D partner believes that this use offers the highest potential returns.
2. *Control of the initial manufacturing process.* Often the processes discovered at the test-tube level must be fundamentally altered as manufacturing is scaled up. The development of manufacturing technologies may also require the release of information not protected by patents.
3. *Control of manufacturing after product approval.* This is a particularly significant right for human therapeutic products. When the US Food and Drug Administration (FDA) approves a new drug, the approval extends only to the particular facility where it is being manufactured. If a pharmaceutical company seeks to move production from the facility of an R&D partner to one of its own, it must undergo another extensive and time-consuming FDA review. Thus, the assignment of manufacturing rights is frequently an item of contention.

Finally, almost all pharmaceutical firms have large sales forces, which engage in the time-consuming process of developing personal relationships with doctors and

²The authors also discuss how if there are multiple innovations, the ownership of individual innovations may be assigned differently, with each party getting property rights to the innovations where it has a comparative advantage in creating value. This theme is explored in considerably greater depth in [Aghion and Tirole \(1997\)](#).

hospital administrators. At least until very recently, most biotechnology firms have sought to develop similar capabilities, in the belief that a sales force would allow them to enhance their profit margins and their strategic position. The final two key control rights thus relate to the marketing of the bio-engineered product:

1. *Retention of all sales categories for financing firm.* This control right allows the financing firm to have primary responsibility for marketing the product in all market segments, whether defined by geography (country) or product (disease indication). If the R&D firm retains primary responsibility for some territories, we do not code the control right as being assigned to the financing firm.
2. *Ability to exclude the R&D firm from all aspects of the marketing process.* This control right allows the financing firm to exclude the R&D firm from all aspects of the marketing process—even from supporting roles—in the US (typically the largest market). Similar to above, if the R&D firm retains some roles, we do not code the control right as being assigned to the financing firm.

In the bulk of the analyses, we examine how many of these key five control rights are assigned to the financing firm. This structure for the analysis is suggested by the legal treatment of technology licenses. Because the licensor (in each case, the R&D firm) contributes the critical intellectual property for the alliance, it reserves any rights that are not explicitly granted to the licensee (Merges, 1995). In some supplemental analyses, we examine a broader group of 25 rights that appear in between 5% and 95% of the agreements. Appendix A lists these additional rights.

The purchase of an equity stake in the R&D firm by the financing firm is not included as a key control right because the equity obtained by the financing firm in these agreements is very modest. In the biotechnology-pharmaceutical firm transactions between 1978 and 1995 in the Recombinant Capital database where an equity purchase was disclosed, the average stake is 9%. The value of the mean purchase (\$7.6 million) is very modest relative to the size of the non-equity payments from the financing firm and (under plausible assumptions) to the expected value of the cash flows to the financing firm from the product under development. The decision to finance part of the transaction as equity appears to be driven by the fact that the financing firm can write off equity investments over a number of years, unlike R&D payments (which must be expensed).

One concern with our analysis is the extent to which the allocation of individual control rights is independent. If these rights are essentially included on an all-or-nothing basis, it might distort our interpretation of the results. There are relatively few cases where two rights appear closely in tandem. Of the 300 pairs, only in ten cases does one control right appear at least two-thirds of the time when the other control right does, and vice versa. Correlation coefficients are generally positive but modest in magnitude. The average correlation coefficient between the five key control rights is 0.026.

Second, the Aghion-Tirole model assumes a one-time contracting process between the two parties. Actual alliances reveal more complex contracting patterns. For instance, pairs of firms undertake repeated sets of alliances on different projects. These successive interactions can lead to increased trust between the two parties and

fewer concerns about the R&D firm providing diminished effort (Banerjee and Duflo, 2000). To partially address this situation, we control for alliances in which the firms have a prior contractual relationship.

Finally, the Aghion-Tirole model assumes that the two parties are sharply differentiated. In actuality, some of the alliances are between pairs of biotechnology concerns. In such cases, both firms may face financial challenges, and consequently these pressures may have no impact on the control right allocation. Furthermore, in these and other alliances, both firms can contribute knowledge. We control, at least partially, for these contingencies by identifying proxies for alliances that are likely to have such horizontal elements. We also repeat the analysis without these agreements.

We examine four questions suggested by theory:

- *Whether during certain periods, the R&D firm has little ability to finance the research by issuing equity and instead turns to alliance financing.*
- *Whether the allocation of control rights differs in agreements that are signed in periods with little external equity financing activity.* When no external equity financing is available, biotechnology firms are likely to have little bargaining power. As argued above, theory suggests that they will more frequently cede control to the financing firm in these instances.
- *Whether success rates differ in agreements that (i) are signed in periods with little external equity financing availability and (ii) cede the bulk of the control to the financing firm.* The theory suggests that the agreements signed in the periods with little external equity financing availability are less likely to maximize innovative output. In particular, in some of the agreements signed during periods with little external equity financing, the R&D firm should cede control when innovation would have been maximized had it retained control.
- *Whether the less attractive agreements are renegotiated.* If the availability of equity from the external market improves dramatically, we should expect that the subset of agreements that assign most of the control to the financing firm are disproportionately renegotiated.

4. The data

4.1. The firm-level data

In the initial analysis, we consider the choice between financing projects through alliances and the firm's own funds (raised from the capital markets). To undertake this analysis, we examine the financing of R&D by 49 biotechnology firms between 1981 and 1993. The sample consists of the largest initial public offerings of pharmaceutical- and therapeutic-oriented biotechnology firms between 1980 and 1989 based on inflation-adjusted market capitalization at the close of the first day of trading. Firms are included in the sample from the year after which they went public either until they are acquired or liquidated or until 1993. Thus, we do not believe that survivorship bias is a significant issue. We focus on publicly traded entities because

we need detailed income statement and balance sheet data for this analysis. We choose the largest firms because their reporting of accounting data is typically much clearer. There is a significant gap between the size of the 49th and 50th largest firm, which led to the use of this breakpoint.

Because R&D is a primary activity for many biotechnology firms, the information about these expenditures is carefully reported in securities filings. In particular, both total R&D expenditures and payments for contract research are typically reported in the footnotes to securities filings. From the financial statements of these firms and the databases of Recombinant Capital, a San Francisco-based consulting firm specializing since 1988 in tracking the biotechnology industry, we determine the total sum of payments for contract R&D each year³ (usually from pharmaceutical and larger biotechnology concerns), and the total annual amount of R&D spending. Because very few biotechnology companies have sustained profitability from operations, the internal R&D spending of these firms is typically from public equity offerings or those by affiliated R&D financing organizations.

We also collect a variety of other measures, which control for the changing information environment and other factors:

- *The number of years that the firm has been publicly traded.* The longer a firm is publicly traded, the longer that investors have had to understand its business and assess the credibility of its management team. All else equal, such a firm should have reduced information asymmetries. A similar measure, firm age, is used as a proxy for publicly available information by [Petersen and Rajan \(1994\)](#).
- *The firm's size, as measured by equity market capitalization plus the book value of outstanding debt.* This measure has been used as a proxy for information problems in such papers as [Hertzel and Smith \(1993\)](#), [Korajczyk et al. \(1991\)](#), and [Pagano et al. \(1998\)](#).
- *The firm's returns in the previous year.* Firms that have experienced positive stock returns have been shown to find it easier to subsequently issue equity (e.g., [Asquith and Mullins \(1986\)](#), [Masulis and Korwar \(1986\)](#), and [Mikkelson and Partch \(1986\)](#)). The revelation of good news about the firm's prospects may increase both the stock price and investors' willingness to provide capital. [Lucas and McDonald \(1990\)](#) show that an information-based model can also explain this pattern.
- *The inverse of the firm's "survival time."* Analyses of the public equity issuance decision typically use the level of debt as an indicator of the danger of costly financial distress (e.g., [Mackie-Mason and Jeffry, 1990](#)). Since almost no biotechnology firm during this period has a significant level of debt, this type of measure is not appropriate. But the danger of distress can be captured by computing the time that the firm can continue without seeking additional financing or cutting back its research activities. For firms that are losing money, the survival time is computed as the ratio of the company's financial reserves

³The precision of this variable is limited to the extent that some of the funds in these contracts are used for purposes other than R&D or that other payments by pharmaceutical firms (in particular, purchases of equity) generate funds that are ultimately used for research.

(defined as the sum of cash, long-term liquid assets, and off-balance-sheet cash held in R&D limited partnerships at the end of the previous calendar year) to the absolute value of the net income in the previous year. Firms that are profitable or running on a breakeven basis are considered to have an infinite survival time (hence, the inverse is zero).

- *The volume of equity raised by biotechnology firms in the previous year.* We compute this in two ways: totaling public equity financings (since this is the alternative most frequently employed by already-public biotechnology concerns) and all equity financing.

Panel A of Table 1 summarizes the firm-level data set. While the average firm finances twice as much of its R&D on its own as through relationships with other firms, the ratio is considerably smaller for the median firm. The financial measures are quite skewed, with a few R&D firms much more established than the others.

Table 1

Characteristics of the samples

Panel A summarizes the first sample, which consists of a panel of the 49 largest (by inflation-adjusted market capitalization at the close of the first trading day) pharmaceutical- and therapeutic-oriented biotechnology firms that went public between 1980 and 1989, observed annually between 1981 and 1993. Panel B summarizes the second sample, which consists of 200 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980–1995 period. The stage of product, focus of alliance, and characteristics of pairs of firms in alliance measures are all dummy variables. The financial condition, firm value, equity raised, and alliance payment variables are expressed in millions of 1995 dollars. The date variable is expressed as a decimal (e.g., July 1, 1995 is coded as 1995.5).

Variable	Mean	Median	Stan. Dev.	Minimum	Maximum
<i>Panel A: Panel of 49 leading biotechnology firms</i>					
R&D funding from other firms in prior year	5.92	2.43	9.71	0.00	64.20
Self-funded R&D in prior year	12.08	3.38	31.47	0.00	265.40
Net income in prior year	−2.81	−2.99	31.60	−122.90	466.40
Cash and other liquid assets at end of prior year	25.37	8.67	49.66	0.23	426.00
Firm's equity return in prior year	0.26	−0.02	0.99	−0.80	7.22
Years firm has been publicly traded	5.32	5	3.15	1	13
Firm value (equity market value plus debt)	321.83	96.21	954.80	0.22	10926.48
Public biotech equity raised in prior year	685	287	1177	0	4598
All biotech equity raised in prior year	1026	612	1253	77	5107
<i>Panel B: 200 technology alliances</i>					
Variable					
<i>Stage of Lead Product at Time of Alliance:</i>					
Discovery/lead molecule	0.64			0	1
Pre-clinical development	0.21			0	1
Undergoing regulatory review	0.15			0	1
<i>Focus of Alliance:</i>					
Human therapeutics	0.92			0	1
Human diagnostics	0.04			0	1
Agricultural or chemical applications	0.04			0	1

Table 1 (continued)

Variable	Mean	Median	Stan. Dev.	Minimum	Maximum
<i>Condition of Financing Firm:</i>					
Revenues in prior year	8912	5218	18649	1	179601
R&D expenditures in prior year	588	457	499	2	1958
Net income in prior year	645	473	623	-457	2232
Cash flow from operations in prior year	970	668	943	-448	5234
Cash and equivalents at end of prior year	1048	644	1066	1	4938
Total assets at end of prior year	7765	5716	8210	1	53632
Shareholders' equity at end of prior year	3738	2851	3569	0	17505
<i>Condition of R&D Firm:</i>					
Revenues in prior year	11	0	80	0	1029
R&D expenditures in prior year	9	5	16	0	171
Net income in prior year	-6	-5	14	-65	134
Cash flow from operations in prior year	-5	-5	18	-62	171
Cash and equivalents at end of prior year	16	8	26	0	229
Total assets at end of prior year	36	14	111	0	1079
Shareholders' equity at end of prior year	25	11	68	-17	665
Age of R&D firm	5	4	3	0	36
<i>Characteristics of the Alliance</i>					
Date of alliance	6/91	12/91	3.1 years	1/80	12/95
Minimum length of R&D alliance (years)	3.79	3.00	2.65	0.75	31.00
Total pre-commercialization payments	29.01	21.42	28.94	0.19	216.28
Payment at the time of signing	1.76	0.51	3.02	0.00	12.00
Previous alliance between firms?	0.06			0	1
Control rights given to financing firm (out of 5)	2.81	3	1.10	0	5
Control rights given to financing firm (out of 25)	9.22	9	2.68	0	16

4.2. The contract-level data

One advantage of studying biotechnology firms is the degree of disclosure in this industry. Publicly traded biotechnology firms, like other concerns, are required by the US Securities and Exchange Commission (SEC) to file material documents. Biotechnology companies tend to interpret this requirement conservatively, and often file alliance contracts. This willingness to file reflects the facts that biotechnology firms typically derive little income from sales and that payments as part of alliances represent a large share of their total revenues.

As of December 1998, Recombinant Capital had identified over 7,000 biotechnology alliances by examining securities filings with federal and state authorities, news accounts, and press releases, and had analyzed about 900 of the approximately 4,800 alliances that had been filed with the SEC or other government bodies. When performing analyses, Recombinant Capital seeks to verify any information obtained from the filed alliances by examining subsequent filings by the firms. (Firms can request confidential treatment for key information, but nondisclosure can become an issue if the firm is sued for security law violations; shareholder class-action litigation has occurred frequently in high-technology industries.) The Recombinant Capital database is typically licensed by major

pharmaceutical, accounting, and law firms for a considerable annual fee, and had not been made available to academics prior to the inception of this project

For our analysis, we select a random sample of 200 of the analyzed alliances. We seek to create a population that avoids undesirable heterogeneity. In particular, we eliminate alliances where:

- One of the parties is a university, medical center, non-profit organization, or government agency.
- One of the parties has a controlling interest in the other, either through a majority equity stake or through a purchase option (e.g., an alliance between a firm and one of its R&D limited partnerships).
- The two parties have a previous alliance covering the same set of technologies, and consequently are renegotiating the terms of an earlier alliance.
- There is neither a research nor a product development component, but the alliance simply involves the marketing of an existing product.
- More than two firms are involved, making the analysis of the contract less tractable.
- The agreement as filed contains information on neither the duration of the alliance nor the structure of the payments between the two firms.
- The agreement is signed after 1995, so that it is difficult to analyze alliance outcomes.

Because determining the circumstances of alliances requires considerable research, we do not eliminate the agreements before assembling the random sample. Rather, we first draw a random sample of agreements. When we discover that an alliance violates one of the criteria, we eliminate the observation, and randomly draw another alliance to bring the sample size back up to 200.

Although alliances between two biotechnology companies might be thought to be collaborations between equals rather than transactions with a well-defined financing firm as the theory depicts, in the median such alliance the larger biotechnology firm has 138 times the revenues and 40 times the shareholders' equity of the smaller one. In each case, the cash flows are unidirectional. (One contract adds some contingencies for the smaller firm subsidizing research at the larger firm; eliminating this case has little impact on the results.)

A comparison of the alliances in the sample with the universe of filed agreements, as well as the subset summarized by Recombinant Capital, highlights the fact that our criteria disproportionately eliminate several classes of agreements. The Recombinant Capital database includes a variety of contracts, such as licenses of approved products and diagnostic kits, which do not meet the definitions above. The observations in the sample are concentrated towards the later years of the sample. This reflects not only the increasing level of alliance activity in recent years, but also Recombinant Capital's propensity to summarize more recent alliances, due to their greater relevance to its clients. (The 49 firms in the sample discussed in Section 4.1. represent 26% of the alliances in the sample of 200 transactions.)

Using the Recombinant Capital database, we code several variables. The first of these is the number of control rights assigned to the financing firm. A value of one

indicates that the particular right is allocated to the financing firm, and zero if not. We also wish to control for the scale of alliance. We thus compute the sum of all pre-commercial payments that the financing firm commits to make as part of the alliance (some of these may be contingent on the achievement of technological or regulatory targets), the size of the up-front payment, and the minimum alliance duration.

For each of the 200 alliances, we gather a variety of supplemental data. First, we determine from the Recombinant Capital database the nature of the regulatory review facing the technology. The review of new human therapeutics by the FDA is frequently exhaustive, often stretching for a decade or longer. Agricultural and chemical bio-engineered products face somewhat less arduous reviews, as do diagnostic products.

Second, we identify the progress of the lead product in the alliance. The Recombinant Capital database identifies—and we corroborate from SEC filings and press accounts in the LEXIS-NEXIS and Dow Jones News Service databases—the stage of the lead product candidate covered by the alliance in the regulatory approval process at the time of the signing. (The stages are summarized in Appendix B.)

Third, we examine the prior relationship between the two parties in the alliance. Using Recombinant Capital's database, which lists all alliances disclosed in securities filings, press releases, or other news accounts, we determine whether the two firms had any previous alliances. While, as discussed above, we eliminate observations from the sample where the two parties have a previous alliance covering the same set of technologies, in some instances they have an alliance in a different area.⁴

Fourth, knowledge spillovers from other R&D projects can have an important impact on the success of an R&D project. We thus compile the overall research spending of the R&D firms. We determine these data from the Compustat and Worldscope databases for the end of the fiscal year immediately prior to the alliance. When this information is not available from Compustat or Worldscope, we gather the information from 10-K filings, IPO prospectuses, and other securities filings.

Fifth, to determine the outcome of the lead product in the alliance, we employ a variety of information sources. Recombinant Capital has compiled a large number of press releases and securities filings about alliances and a database of all pharmaceutical products under development by biotechnology firms. We also search SEC filings and news stories in the LEXIS-NEXIS and Dow-Jones News Service databases. Finally, we use two specialized databases, IMS and PharmaProjects, that track the development of pharmaceutical and bio-engineered products through monthly surveys of firms as well as reviews of FDA filings. While these databases have some limitations—in particular, firms may not always disclose strategically important pre-clinical projects—industry executives believe that they give a fairly comprehensive picture of drugs in the clinical stages of development.

⁴One concern is that information on earlier transactions might be substantially less complete in the early years of the sample. Biotechnology firms typically file information about all their earlier alliances when they go public, allowing Recombinant Capital to accurately ascertain these firms' previous alliances, even for the earlier periods when they were not collecting press releases and other information.

We find information on alliance renegotiations in the Recombinant Capital database (which notes such renegotiations in its alliance summaries and compiles press releases announcing renegotiations), SEC filings, and press accounts in the LEXIS-NEXIS and Dow Jones News Service databases. Using the same sources, as well as industry-specific directories such as [Dibner \(1999\)](#), [Ernst and Young \(1996\)](#), and [Oryx Press \(1996\)](#), we identify public equity financings by biotechnology firms, and compute the inflation-adjusted amount of funds raised in the quarters prior to the alliance. We construct two alternative measures of equity financing activity, the dollar volume of all public equity offerings by biotechnology firms and the dollar volume of all equity raised by biotechnology firms. (The difference between the two series is largely due to venture capital transactions.)

Panel B of [Table 1](#) summarizes the alliances and the firms entering into these agreements. Several patterns can be observed from these summary statistics. Most alliances are undertaken at a very early stage, well before the commencement of clinical trials. The disparity between the financial conditions of financing and R&D firms is substantial, with the average financing firm having several hundred times the revenues and assets of the mean R&D firm. The mean R&D firm's operating cash flow is sufficiently negative that it would exhaust its cash and equivalents in about three years' time (if the losses continue at the same level and no additional financing were received). The assignment of control rights to the financing firm is highly variable.

5. Empirical analyses

5.1. Relation between financial market conditions and subsequent R&D financing

Before considering the predictions of Aghion-Tirole model, it is appropriate to explore its key assumption. How reasonable is the claim that during periods with little external equity financing, the bargaining power in alliance negotiations shifts in favor of pharmaceutical firms?

The analysis in this section is related to the hotly debated topic of the impact of capital constraints on investment. Modern studies (reviewed in [Hubbard, 1998](#)) typically seek to relate investment to cash flow for subsets of firms that have been a priori identified as capital constrained or unconstrained through some objective criteria. The greater sensitivity of the investment by constrained firms to cash flows is interpreted as indicating that the firms are capital constrained, though this interpretation is not uncontroversial ([Kaplan and Zingales, 1997](#)). Unfortunately, such an approach would not lend itself to the biotechnology industry. First, it would be difficult to think of criteria that would lead to the identification of a set of unconstrained biotechnology firms. Moreover, the very notion of cash flow shaping investment in this industry does not seem reasonable, since virtually all firms were losing a substantial amount of money during the 1980s and early 1990s. Rather, the rate of R&D is determined by firms' existing supply of funds and their expected ability to raise capital in the future.

We thus focus in this analysis on the shifting sources of R&D financing. For our panel of 49 biotechnology firms, we divide each firm's spending on R&D into that financed by pharmaceutical firms and that self-financed on an annual basis.⁵ We examine whether periods with substantial information asymmetries—as proxied by reduced equity offerings—lead firms to shift from relying on the public markets for financing to raising capital from informed intermediaries such as pharmaceutical companies.

The first two columns of [Table 2](#) present a regression analysis of the mixture of financing sources for R&D expenditures. The dependent variable is the share of R&D funded by pharmaceutical firms. The independent variables are the firm's financial health (measured by the inverse of the survival time), the extent of information asymmetries surrounding the firm (measured by the number of years the firm has been publicly traded and its size), the firm's stock return in the past year, and a measure of equity financing raised by biotechnology companies in the previous year (either the volume of equity raised in the public market by biotechnology firms or the total equity financing raised by these firms).

The coefficients of the measures of equity raised, -0.04 and -0.04 , suggest that increases in external equity financing lead firms to increasingly self-finance research, and vice versa. The magnitude of the effect, however, is modest. At the mean of the independent variables, a doubling of the external financing raised by biotechnology firms decreased the predicted share of R&D financed by pharmaceutical companies in the next year from 44% to 41%. Consistent with the interpretation offered above, characteristics associated with greater firm-level information asymmetries (e.g., firms with a shorter history as publicly traded entities and of smaller size) also lead to a greater reliance on pharmaceutical firms for financing.

The third and fourth columns report the results of two checks of the robustness of the results. We add an estimation using fixed effects, as well as one employing an AR(1) autocorrelation term, which is allowed to take on a different value for each firm in the sample. While the sign is the same, the coefficient of the measure of equity financing, -0.02 , is no longer significant in the regression employing fixed effects, although it remained significant when we added the autocorrelation term.

In unreported regressions, we examine the determinants of the dollar amount of pharmaceutical- and self-funded research. The amount funded by pharmaceutical companies does not vary significantly with the proxies for information asymmetries: only the measure of financial health (the inverse of the survival time) is significant. Self-financed R&D, on the other hand, varies in a highly significant way with the maturity of the firm and the state of the public equity market. Apparently concerned about their ability to raise additional capital from public investors in these environments, biotechnology firms cut back on their own financing of R&D.

⁵ Observations at higher frequencies are precluded by the nature of the reporting of these expenditures, as well as the unevenness in corporate payments. The self-financed portion is largely from the firms' own cash reserves, which are typically raised from equity investors. (Some of the funds are from R&D financing organizations, which, while technically freestanding entities, are controlled by the firm.)

Table 2

Sources of R&D funding

The sample consists of a panel of the 49 largest (by inflation-adjusted market capitalization at the close of the first trading day) pharmaceutical- and therapeutic-oriented biotechnology firms that went public between 1980 and 1989, observed annually between 1981 and 1993. The dependent variable is the ratio of pharmaceutical-funded R&D to total R&D expenditures in the calendar year. The independent variables are the ratio of the absolute value of the firm's net income in its previous year to its liquid assets at the end of the year (firms at breakeven or with positive net income at the end of the year are coded as zero), the company's stock return in the previous year, the years that the firm had been publicly traded, the firm's value (market value of equity and debt) at the end of the previous year, and either the volume of equity raised in the public market by biotechnology firms in the previous year or the total equity financing raised by these firms. (The last three are in billions of 1995 dollars). The third regression employs fixed effects; the fourth regression a firm-specific AR(1) correction. All regressions employ ordinary least squares specifications. Heteroskedastic-consistent standard errors are in brackets except in the last regression, where standard errors are reported.

	Dependent variable: Ratio of pharmaceutical to total R&D			
1/(Survival time)	0.003 [0.004]	0.003 [0.004]	*0.01 [0.004]	0.003 [0.003]
Stock return in past year	-0.02 [0.02]	-0.02 [0.02]	-0.03 [0.04]	*-0.03 [0.02]
Years firm has been publicly traded	** -0.03 [0.01]	** -0.02 [0.01]	-0.03 [0.02]	*** -0.03 [0.01]
Firm value (1995 \$ billions)	** -0.03 [0.01]	** -0.03 [0.01]	** -0.06 [0.02]	-0.02 [0.03]
Public biotech equity raised (1995 \$ billions)	** -0.04 [0.02]		-0.02 [0.03]	** -0.04 [0.02]
Total biotech equity raised (1995 \$ billions)		** -0.04 [0.02]		
Constant	*** 0.62 [0.08]	*** 0.63 [0.08]		*** 0.66[0.07]
R ²	0.05	0.05	0.43	
p-Value of regression	0.000	0.000	0.000	0.001
Number of observations	309	309	309	307
Fixed effects?	No	No	Yes	No
Firm-specific AR(1) term?	No	No	No	Yes

Note: The sample size is smaller for the AR(1) specification because two observations are dropped which were the only observation of that firm. The constant is not reported in the fixed-effects regression, because its interpretation is unclear.

***Significant at 1% confidence level.

**Significant at 5% confidence level.

*Significant at 10% confidence level.

In other unreported analyses, we also show that the results are robust to other proxies for firm-level information problems. For instance, we demonstrate substantial differences between cases where the firms have pending applications with the FDA (which are likely to have substantial information asymmetries) and those where new drugs have just been approved (where the gaps are likely to be substantially lessened). We also rerun the regressions, adding some of the controls employed by [Choe, Masulis, and Nanda \(1993\)](#). These changes do not have a significant impact on the results.

While these findings are suggestive, they are certainly not conclusive. In particular, this empirical pattern could be driven by a mechanical relation in which firms that have more cash simply finance their R&D internally without considering alternative sources of funding. Such a “pecking order” story would lead to a similar empirical pattern: after a period of many equity issues, more biotechnology firms would be cash-rich, and fund research with internal funds.

5.2. Relation between financial market conditions and control rights

We next examine the allocation of control rights in a regression framework. The dependent variable is the number of control rights allocated to the financing firm. As discussed above, we focus on five critical control rights.

We employ two specifications for our analysis, estimating both ordinary least squares (OLS) and ordered logit regressions. The latter specification avoids some of the problems associated with the differing importance of the various control rights. Such a regression methodology treats an alliance assigning four control rights to the funding party as more favorable to the financing firm than one with two such control rights, but not necessary twice as favorable.

In the basic specification, we use as independent variables a dummy variable denoting early stage projects at the time of the alliance signing (those projects between the earliest discovery stage and pre-clinical research), the amount of equity collectively raised by biotechnology firms from the public markets in the previous quarter, and a measure of the financial resources of the R&D firm (shareholders' equity). All financial variables are expressed in billions of 1995 dollars. (We are missing balance sheet data for about 10% of the alliances, typically alliances signed while the firms were still private.) In supplemental regressions, we add controls for the nature of the agreement, including dummy variables denoting whether the agreement focused on agricultural, chemical, or diagnostic biotechnology, whether the alliance was between two biotechnology firms, and the count of patents in related fields awarded to the R&D firm.

The basic analyses are reported in [Tables 3](#). The firm-specific measures suggest that, consistent with the Aghion-Tirole hypothesis, an R&D firm in a stronger financial position retains more of the control rights in the alliance. For example, in the first regression, a one standard deviation increase in the R&D firm's shareholders' equity at the mean of the independent variables leads to a drop in the predicted number of control rights assigned to the financing firm from 2.9 to 2.7 rights (two-tenths of a standard deviation of this measure). (This effect is weaker and less significant when additional control variables are added.) Similarly, projects that are in their early stages, which are likely to have a greater need for financing and greater information asymmetries that deter uninformed equity investors, are associated with a significant transfer of control (about one-half of a right) to the financing firm.

The measures of external market conditions display a consistent picture with the firm-level data. During times when public biotechnology equity financing activity in the previous quarter is greater, fewer control rights are likely to be assigned to the financing firm. The coefficients, -0.31 and -0.30 in the OLS regressions and -0.62 and -0.59 in the ordered logit estimations, are significant at the 5% confidence level across all the regressions. Consistent with the theory and the firm-level patterns, R&D firms in weaker markets cede more control rights. A time trend in control rights could confound these results. For instance, financiers might have gradually learned about opportunistic behavior that biotechnology firms could undertake, and added new protective clauses. In actuality, there is a negative correlation between the

Table 3

The allocation of control in alliances

The sample consists of 200 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980–1995 period. The dependent variable is the number of control rights (out of five rights identified in conversations with practitioners) assigned to the financing firm. The independent variables are a dummy variable indicating if the lead product was not yet in clinical trials at the time of the alliance, the shareholders' equity of the R&D firm, and the total volume of public equity financing raised by biotechnology firms in the previous quarter. In two supplemental regressions, additional variables include dummies denoting if the agreement involved the development of an agricultural or chemical product, the development of a diagnostic product, or two biotechnology companies, and the number of related patents awarded to the R&D firm at the time of the agreement. All financial variables are in billions of 1995 dollars. The first two regressions employ ordinary least squares specifications; the second two, ordered logit specifications. Standard errors are in brackets.

	Dependent variable: Control rights assigned to financing firm	
	OLS specification	Ordered logit specification
Was lead product not yet in clinical trials at alliance signing?	***0.50 [0.17]	***0.84 [0.32]
R&D firm's shareholders equity (1995 \$ billions)	** -1.91 [0.86]	** -4.12 [2.07]
Public equity raised by biotechnology firms in previous quarter (1995 \$ billions)	** -0.31 [0.14]	** -0.62 [0.27]
Did agreement focus on agricultural or chemical product?	0.19 [0.39]	0.29 [0.65]
Did agreement focus on diagnostic product?	0.36 [0.34]	0.86 [0.65]
Was agreement between biotechnology firms?	-0.22 [0.20]	-0.34 [0.39]
Number of related patents awarded to R&D firm	0.01 [0.02]	0.001 [0.029]
Constant	***2.60 [0.16]	
Adjusted R^2 or Pseudo R^2	0.11	0.10
p -Value of regression	0.000	0.001
Number of observations	180	180

***Significant at 1% confidence level.

**Significant at 5% confidence level.

*Significant at 10% confidence level.

assignment of control rights to the financing firm and time, although it is not a robust one.

We explore the robustness of these results in several unreported regressions:

- The review process that agricultural, chemical, and diagnostic biotechnology products undergo is quite different from that of therapeutics, which constitute the bulk of the sample. While we attempt to control for these differences in the regression above through the use of dummy variables, it may be inadequate. We repeat the analysis, simply using therapeutic products.
- We eliminate all agreements between two biotechnology firms, rather than between biotechnology and pharmaceutical concerns, as in these cases the assumption that the financing party only contributes capital to the alliance is less tenable.
- Because venture financing became increasingly common during this period, its omission may give a misleading impression. We repeat the analysis, including the volume of private equity financing in the measure of equity financing cycles.
- The measures above compute financing activity only within the past quarter. Given the “lumpiness” in financing activity (a single offering accounts for the bulk of public equity activity in some quarters), this measure may be prone to an errors-in-variable problem. We repeat the analyses using financing activity over the past four quarters.
- Rather than focusing on the five control rights identified in conversations with practitioners, we repeat the analyses, assuming that all 25 control rights identified in Appendix A are equally important.

In all but one case, firm-level financial strength and stronger overall financial market conditions for biotechnology firms continue to be associated with the biotechnology firm retaining more control at least at the 5% level of statistical significance. When we use the measure of 25 control rights, however, the association between strength of financial markets and control assigned to the biotechnology firm is no longer significant at conventional confidence levels.

5.3. *Relation between financial market conditions and alliance outcomes*

We next examine whether agreements that cede the bulk of the control to the financing firm and are signed in weak financing markets prove less successful. By focusing on the *interaction* between the financing environment and the control right allocation, we limit the danger of drawing false inferences. For instance, agreements assigning the bulk of the control to the R&D firm might be more successful because the projects are of higher quality in some unobservable way. Similarly, agreements signed when substantial external financing is available might be more successful if the greater ability of firms to raise equity financing reflects the fact that there are many attractive opportunities to exploit, or less successful if in these periods, pharmaceutical companies face an adverse selection problem and only are able to fund the less attractive projects, as [Pisano \(1997\)](#) argues. The ability of these

alternative explanations to explain the interaction of these variables, however, is less obvious.

Table 4 takes a first look at the outcomes of the alliances. Panel A reports the status of the lead compound in the alliance as of the end of 1998. Observations are divided by their status at the time the agreement was signed. Note that the time that

Table 4

Outcome of alliance agreements

The sample consists of 200 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980–1995 period. Each column of Panel A reports, for alliances in various stages at the time of the agreement, the progress of the lead product in the alliance at the end of 1998. Cases where the lead product has already begun field or human trials are excluded from the “Not Yet in Trials” and “At Least in Phase I Trials” tabulations. In the “At Least in Phase I Trials” tabulation, cases where field or human trials of agricultural, chemical, and diagnostic products where there is no distinct staging of the trials have begun are also coded in the affirmative. Agreements where the lead therapeutic product was in Phase III trials or awaiting regulatory approval or involving agricultural, chemical, or diagnostic products are excluded from the “At Least in Phase III Trials” tabulation. Panels B and C report the percentage of agreements reaching each stage for alliances where four or more control rights assigned to the financing firm (out of the key five rights) and three or fewer rights were assigned to the financing firm, as well as the results of a χ^2 -test assessing the significance of these differences. In Panel B, the analysis is confined to observations where the level of public equity issuance by biotechnology firms in the four quarters before the alliance was signed was below the median. In Panel C, the analysis is confined to those where the equity issuance by biotechnology firms was above the median. In the “At Least One Step Further” tabulation, cases where the lead product in the alliance began trials (for agreements where the lead product was not yet in trials at the time of the alliance signing), entered Phase III trials (for agreements where the lead therapeutic product was in Phase I or II trials), or was approved (for agreements where the lead therapeutic product was in Phase III trials or awaiting regulatory approval, or for agricultural, diagnostic, or chemical products undergoing trials) are coded in the affirmative.

Panel A: Summary of entire sample

	Status in December 1998				
	<i>Not yet in trials</i>	<i>At least in Phase I trials</i>	<i>At least in Phase III trials</i>	<i>Approved</i>	<i>Number of observations</i>
<i>Status at Time of Signing</i>					
Discovery	69%	31%	12%	5%	86
Lead molecule	38%	62%	10%	10%	42
Pre-clinical or formulation Phase I or II	26%	74%	33%	19%	42
Phase III or under final review			65%	26%	23
Share of possible transactions ^a	51%	49%	27%	71%	7
Number of observations	86	84	52	27	200

Panel B: Agreements signed in unfavorable biotechnology financing markets

	Status in December 1998			
	<i>At least in Phase I trials</i>	<i>At least in Phase III trials</i>	<i>Approved</i>	<i>At least one step further</i>
Share successful, “pro financing firm” alliances	47%	22%	16%	50%
Share successful, “pro R&D firm” alliances	67%	42%	23%	70%
χ^2 statistic from test of difference	3.37	3.73	0.669	3.60
<i>p</i> -Value, χ^2 test	0.066	0.053	0.413	0.058

Table 4 (continued)

	Status in December 1998			
	<i>At least in Phase I trials</i>	<i>At least in Phase III trials</i>	<i>Approved</i>	<i>At least one step further</i>
Share successful, “pro financing firm” alliances	35%	16%	0%	35%
Share successful, “pro R&D firm” alliances	42%	21%	10%	49%
χ^2 -statistic from test of difference	0.41	0.27	3.28	1.66
<i>p</i> -Value, χ^2 test	0.522	0.601	0.070	0.197

^aThe calculation of the share that were not yet in trials in December 1998 excludes those alliances that were already in clinical trials at the time of the alliance signing. The calculations of the share that were at least in Phase I and Phase III trials in December 1998 excludes those alliances that had already advanced to or beyond the stage at the time of the alliance signing.

the products had to advance through the approval process differs considerably: while each of the agreements had been undertaken at least three years earlier, in some cases, the agreement was signed over a decade before. In a number of cases, the agreements between the R&D and financing firm are terminated by the end of 1998. While in most cases, work on the lead molecule ends after the agreement lapses, in some instances the biotechnology company funds further development itself or finds another corporate partner. The termination of alliances developing ultimately successful projects often is a consequence of a corporate merger or shift in strategy. Because of these instances, we measure the ultimate success of the project, rather than the duration of the alliance itself.

A complication in this analysis, as well as that reported in Table 5, is introduced by agricultural, diagnostic, and chemical projects for which there is not a clear stage of the regulatory review process corresponding to Phase III for therapeutic products. In these instances, we examine only whether the project enters the regulatory review process and whether the project is approved. Another complication is the modest number of cases in which the lead product is abandoned or de-emphasized in favor of another product that surpasses the lead product in the regulatory review process. In these cases, we track the status of the most advanced product covered by the alliance.

The table highlights the fact that relatively few products had been approved by the end of 1998. In all, 14% of the alliances result in an approved drug (26% of those that were in Phase I or Phase II trials at the time the alliance was signed). This low success rate is consistent with evidence about the success of pharmaceuticals more generally: for instance, the Pharmaceutical Research and Manufacturers of America (1998, Fig. 3-1) estimates that for every five drugs that entered Phase I clinical trials in recent years, only one was ultimately approved for sale by the FDA.

To examine whether the theoretical suggestions regarding alliance success are borne out in the data, we compare the relation between the assignment of control and success in agreements signed during periods with and without substantial external equity financing by biotechnology firms. We compare four measures of

Table 5
Cox proportional hazard regression analyses of the outcome of R&D alliances

The sample consists of 200 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980–1995 period. The dependent variable in the first regression of Panel A and in Panel B is the time until the lead product began trials (for agreements where the lead product was not yet in trials at the time of the alliance signing), entered Phase III trials (for agreements where the lead therapeutic product was in Phase I or II trials), or was approved (for agreements where the lead therapeutic product was in Phase III trials or awaiting regulatory approval, or for agricultural, diagnostic, or chemical products undergoing trials). The dependent variable in the second regression in Panel A is the time until the lead product in the alliance was approved. The independent variables are dummy variables denoting whether the agreement entails the development of an agricultural or chemical product or the development of a diagnostic product, the stage of the lead product at the time of the alliance (with products in the discovery stage denoted as one and those awaiting regulatory approval as nine), a dummy variable denoting whether the firms had undertaken a previous alliance, the total pre-commercialization payments that the financing firm had committed to as part of the alliance (in millions of 1995 dollars), the total R&D spending of the R&D firm in the year prior to the alliance (in millions of 1995 dollars), a dummy variable denoting if the public equity financing raised by biotechnology firms in the quarter before the alliance signing was above the median, the number of five critical control rights assigned to the financing firm, and the interactions of these two measures. The second panel presents the coefficients of the final three variables in alternative specifications. All regressions employ ordinary least squares specifications. Standard errors are in brackets.

Panel A: Basic specifications

	Dependent variable	
	Time until entering next phase	Time until lead product approval
Did agreement focus on agricultural or chemical product?	1.09 [0.45]	1.16 [0.74]
Did agreement focus on diagnostic product?	0.44 [0.52]	1.09 [0.76]
Stage of lead product at time of alliance	***0.18 [0.04]	***0.39 [0.09]
Did agreement involve two firms with prior alliance?	−0.04 [0.43]	*1.46 [0.76]
Total pre-commercialization payments in the alliance (1995 \$ millions)	**0.007 [0.003]	0.005 [0.006]
Total R&D spending by R&D firm in prior year (1995 \$ millions)	−0.01 [0.01]	−0.02 [0.02]
Was equity financing in previous quarter by biotech firms above median?	−0.07 [0.26]	1.10 [1.07]
Count of five key control rights assigned to financing firm	**−0.24 [0.12]	**−0.38 [0.16]
Interaction between high financing dummy and count of control rights	*0.28 [0.13]	**0.54 [0.25]
p-Value of regression	0.000	0.000
Number of observations	171	171

Panel B: Robustness of key variables to changes in specification (using time until entering next phase as the dependent variable)

	Independent variable	
	Volume of equity financing	Count of control rights
Eliminating deals between biotechnology firms	−0.21 [0.27]	**−0.28 [0.11]
Eliminating non-pharmaceutical transactions	−0.02 [0.27]	**−0.20 [0.10]
Using all 25 control rights	−0.27 [0.32]	*−0.08 [0.05]
Using financing activity over past calendar year	0.38 [0.28]	*0.20 [0.12]
Using all, not just public, equity financing	0.08 [0.26]	**−0.29 [0.14]
		Interaction term
		**0.30 [0.13]
		**0.23 [0.11]
		**0.13 [0.06]
		*0.25 [0.14]
		**0.36 [0.15]

*** Significant at 1% confidence level.
 ** Significant at 5% confidence level.
 * Significant at 10% confidence level.

success in transactions that are more or less favorable to the R&D firm. We contrast these differences in alliances signed in periods where the level of external equity financing in constant dollars is above or below the median.

The results, reported in Panels B and C, suggest that alliances with the fewest control rights assigned to the financing firm have the greatest success. The differences are substantial when the agreement is signed in a poor market. The differences in these four cases average 17% and are statistically significant at the 10% confidence level in three out of four cases. (The one case with no significant differences, that of product approvals, is characterized by a modest number of successes.) For agreements signed in favorable markets, the differences are smaller in magnitude, averaging 9%. The effects are only significant at conventional confidence levels when we use the measure of whether a product is approved. In a variety of unreported tabulations, we explore the robustness of the results to the use of different cutoff points. The magnitude of the differences between the effects in favorable and unfavorable markets for biotechnology firms appears to strengthen when we use either more or less permissive definitions of what constituted a favorable market. When we change the definition of “pro-R&D firm” agreements to include significantly more agreements in this categorization, however, the differences weaken.

While these tabulations can be interpreted as providing some support for the hypotheses in [Aghion and Tirole \(1994\)](#), the comparisons might be misleading due to the different “vintages” of the projects. Consider the possibility that the allocation of control rights in alliances changes over time. A disproportionate number of older alliances, in which the lead product had more time to progress through regulatory reviews, might have assigned few control rights to the financing firms. Clearly, this and other effects can only be addressed through regression analyses.

In addition to the differences in alliance “vintage,” a variety of other factors can affect the success of bio-engineered products. We address a variety of concerns:

- As noted above, the review process of agricultural, diagnostic, and chemical products is frequently less rigorous.
- The probability of ultimate approval, as [Table 4](#) suggests, should increase as the product progresses through the review process. Controlling for the stage of the lead product at the time of the initiation of the alliance is important.
- As noted above, instances where the two parties have undertaken a previous alliance may be subtly different: in particular, the two parties may have more reputational capital at stake, leading to greater effort and more success.
- Finally, [Henderson and Cockburn \(1996\)](#) show—consistent with the well-understood problems in creating markets in innovative products—that economies of scale and scope play an important role in determining the success of pharmaceutical R&D projects. Their empirical and clinical research suggests that not only are larger projects more successful, but so are those at firms with multiple research projects in different areas. We employ two control variables in the reported regressions: the total dollar amount that the financing firm commits to the alliance, as well as the overall R&D expenditures of the R&D firm.

Table 5 presents a variety of regression analyses. In each case, we hypothesize that new biotechnology products are generated through a production function, $Y = F(x, \beta)$, where Y is the probability that a given product is developed, x is a vector of inputs or attributes that influence the discovery process, and β is a vector of coefficients. Since our observations consist of the time until a given product commences trials or is approved, we use a survival model.

We employ a Cox proportional hazard specification, in which the dependent variable is the time until a given outcome. An alliance is assumed to have a certain probability of succeeding in each period. The instantaneous probability of success at any given time t is called the hazard rate, $h(t)$, defined as

$$h(t) = \frac{\text{Probability of success between } t \text{ and } t + \Delta t}{\text{Probability of success } \geq t}$$

More specifically, the Cox model assumes that the hazard function has the functional form $h(t) = H_0(t)e^{\beta_1 x_1 + \beta_2 x_2 + \dots + \beta_N x_N}$. The model is quite unrestricted in the sense that no assumptions are made about the function $H_0(t)$, but it does impose some other restrictions, as will be discussed below.

The first regression in Panel A of Table 5 and those in Panel B estimate the time until the next major milestone in the approval process. We define these milestones as the commencement of clinical or field trials for products that are not yet in trials at the time the alliance is signed, the commencement of Phase III trials for therapeutics that are in Phase I and II trials, and regulatory approval for more advanced cases. We do not use the transition from Phase I to Phase II trials as a milestone here because the commencement of Phase II trials is often not announced in the press releases, securities filings, or in FDA filings. Because Phase III trials are much more extensive (and hence costly), their commencement is much more frequently disclosed. Observations are right-censored at the end of 1998: no data are used after this point. The model addresses the possibility that a success is not observed because of two reasons: either the outcome occurs in 1999 or thereafter, or no success ever occurs. The second regression in Panel A analyzes the time until the approval of the product.

Not surprisingly, in each of the regressions, projects that are further along are more likely to succeed. In the first regression, alliances in which there is a larger funding commitment by the financing firm are also associated with greater success, consistent with earlier results about the importance of scale in research projects. Finally, alliances that assign more control to the financing firm are less likely to lead to successful outcomes.

The coefficients of the interaction terms are positive and approximately equal in absolute magnitude to the control right coefficient, consistent with the predictions of Aghion and Tirole (1994). The two coefficients, 0.28 and 0.54, are statistically significant at the 5% confidence level. They are also economically significant. Consider the leftmost regression. In an alliance signed when biotechnology financing activity is above the median, a shift from three to four control rights assigned to the financing firm has a negligible effect on the hazard rate. But in an alliance signed when financing is below the median, such a shift in control leads to a 21% reduction

($e^{(-0.24)(1 \text{ control right})} - 1 = 0.79 - 1$) in the hazard rate, or probability of success in a given period.

The Cox model does, however, constrain the probability that an event occurs at any given time to be proportional. If the probability that a drug is approved is twice as high in one group as in another, the model assumes that this is the case one, two, or five years after the alliance signing. We examine this assumption of proportional hazards, both jointly for all variables and for the individual independent variables. In neither regression do we reject the proportional hazard assumption at the 5% confidence level in the joint test, or at the 10% level in the test of the interaction term. We do, however, reject the proportional hazard assumption at the 10% confidence level for two independent variables. As a robustness check, we re-estimate these equations using stratified Cox regression estimates, in which we divide the observations into groups on the basis of the variables whose hazard rates appear to vary across time (“Total pre-commercialization payments in the alliance” and “Total R&D spending by R&D firm in prior year”). Each group is allowed to have a different hazard rate. While in some cases, the coefficients of other variables vary across equations, the differences in the coefficient of the interaction variable are minimal.

As reported in Panel B, we undertake a number of robustness checks:

- We eliminate agreements that are between two biotechnology firms, rather than between biotechnology and pharmaceutical concerns.
- We repeat the analysis, eliminating agricultural, chemical, and diagnostic biotechnology products, due to the differences in the review process.
- We repeat the analyses assuming that all 25 control rights identified in Appendix A are equally important.
- We repeat the analyses using biotechnology financing activity over the past four quarters.
- We include the volume of private equity financing in the financing measure.

We present in Panel B the coefficients and standard errors for the three independent variables of greatest interest: the equity financing measure, the control rights measure, and the interaction between these two terms. In each case, the interaction term continues to be positive and significant and of about the same absolute magnitude as the control rights coefficient. Similarly, the control right variable remains negative and of the same magnitude, except when the count of all 25 control rights is used (when the magnitude of the coefficient drops considerably).

One pattern in these regressions, however, is difficult to explain. Consistently across the regressions, the impact of adding additional control rights to the financing firm during periods with above-median biotechnology financing activity is positive though statistically insignificant. (We determine the significance of this effect by examining the coefficient of the control rights variable in regressions employing the subset of observations where financing is above the median in the previous quarter, omitting the “above the median” dummy and the interaction term as independent variables.) This suggests that some parties have not reached the optimal arrangement: these alliances could have been improved by transferring additional

control rights to the financing firm. While the Aghion-Tirole model suggests a mechanism that leads to the R&D firm getting *too little* control in some instances, they do not model a setting where the R&D firm gets *too much* control. Note, however, that the model makes some stark assumptions, such as the absence of any information asymmetries between the parties at the time of the negotiation.

In unreported regressions, we explore the sensitivity of the results to a variety of changes in the specification:

- We include the R&D expenditures of the larger firm as an additional control for the scope of the project. While this reduces the sample size—many foreign firms do not report R&D expenditures—the results are qualitatively similar.
- We address concerns that alliances completed in stronger financing markets are larger, even after controlling for the stated amount of pre-commercialization payments. This might be a consequence of measuring the pre-commercialization payments with error. In particular, some of the contingent milestone payments included in the total may be conditional on remote contingencies and consequently have a low expected value. To address this possibility, we add to the regression two other measures, the minimum period for which the financing firm committed to provide funding and the size of the up-front payment at the time of the alliance signing. Longer alliances and those with larger up-front payments are likely to be larger, even after controlling for the size of the pre-commercialization payments. If the greater success of alliances signed in periods with substantial equity financing is due to their greater scale, these alternative measures should also have considerable explanatory power. The new variables are almost uniformly insignificant and variable in sign, however, while the interaction term is little changed.
- We test whether the results are robust to the addition of a number of variables. We add dummy variables to denote cases in which the financing firm made a prior equity investment into the R&D firm, the location of the firm (to control for the geographic effects identified by Zucker et al., 1998), and the disease targeted by the therapeutic alliances. We add measures of the quality of the biotechnology firm akin to the market-to-book (Tobin's q) ratio often used in financial economics: the ratio of market capitalization to employment and patents at the beginning of the year of the alliance. The results are little changed.

5.4. Relation between financial market shifts and alliance renegotiation

A central argument of this paper is that the superior performance of alliances signed in attractive financing markets reflects the greater flexibility of the contracting parties. When the R&D firm has only weak bargaining power, the control rights may be assigned to the financing firm even if assigning them to the R&D firm would generate the most innovation.

One implication relates to the renegotiation of alliances. Agreements in which the optimal division of control rights cannot be achieved should be more frequently renegotiated if conditions change. This suggests an empirical test based on the

overall financing environment for biotechnology firms, which, as suggested above, is subject to dramatic changes. We examine whether the agreements are renegotiated prior to the minimum life stipulated in the agreement. We hypothesize that pro-financing company agreements would be more likely to be renegotiated during periods when the external financing environment for biotechnology firms improves considerably, which is likely to be associated with a shift in bargaining power.

The mean (median) minimum contractually specified alliance length is 3.1 (3.0) years for agreements signed in periods when public equity issuance in the previous 12 months is above the median. For other agreements, the mean minimum specified life is 3.6 (3.0) years. The difference in means is only significant at the 20% confidence level. Moreover, two-thirds of this difference is due to a single agreement signed in the early days of the biotechnology industry, which called for a 31-year alliance. Thus, it appears that the differences in agreements signed in these periods do not affect the results below.

Table 6 presents two regression analyses of the likelihood of premature renegotiation. (Only agreements whose scheduled completion date is prior to January 1, 1999 are included in the regressions, leading to a slightly smaller sample size.) The dependent variable is a dummy that takes on the value one if the alliance is renegotiated prior to its scheduled completion date. The first regression employs as independent variables dummies that denote whether the agreement assigned four or more key control rights to financing firm, whether there is an above-the-median improvement in the financial markets after the agreement is signed (defined as the difference between the inflation-adjusted dollar volume of equity offerings by biotechnology firms in the fifth through eighth quarters after the alliance signing and the four quarters prior to the alliance signing), the interaction between these variables, and a variety of controls. The timeframe is motivated by the fact that the mean prematurely renegotiated agreement is revised 1.96 years after the original agreement. The median time is 1.83 years and the inter-quartile range from 1.25 to 2.5 years. The table also presents the standard errors of the coefficient, and the corresponding odds ratio.⁶

In this regression, the coefficient of the interaction term, 0.40, is significantly positive: during periods of increased biotechnology financing activity, pro-financing company agreements are more likely to be renegotiated. Keeping the other independent variables at their means, the predicted probability of renegotiation of pro-R&D firm agreements when the financing activity does not subsequently increase is 37%. For pro-financing firm agreements that are followed by an upsurge in financing activity, the probability is 58%.

In the regression in the second column of Table 6, we express the external equity financing raised (and the interaction term) as continuous variables. Once again, the coefficient of the interaction term, 0.20, is significantly positive. In the third regression, we delete cases in which either the R&D or the financing firm were

⁶The odds ratio is the number by which we would multiply the odds of an alliance being renegotiated for each unit increase in the independent variable. An odds ratio greater (less) than one indicates that the probability increases (decreases) when the independent variable does.

Table 6

Logit regression analyses of the premature renegotiation of R&D alliances

The sample in the first two regressions consists of 160 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980–1995 period, in which the scheduled expiration of the alliance was by the end of 1998. The sample in the third regression also excludes those transactions where the financing or R&D firm was acquired or merged before the minimum period stipulated in the alliance. The dependent variable is a dummy, where 1.0 denotes an alliance that was renegotiated before the minimum period stipulated in the contract. The independent variables are a dummy variable denoting whether the agreement involved the assignment of four or more control rights to the financing firm (out of the five key rights), a dummy variable denoting whether the change in the financial markets after the agreement (defined as the difference between the inflation-adjusted dollar volume of equity offerings by new biotechnology firms in the fifth through eight quarters after the alliance signing and the four quarters prior to the alliance signing) was above the median or the dollar volume (in billions of 1995 dollars) of this difference, an interaction between the control rights variable and the financing change variable, the date of the alliance (July 1, 1992 expressed as 1992.5, etc.), the age of the R&D firm at the signing of the alliance (in years), and dummy variables denoting whether the financing or R&D firm were acquired or merged before the minimum period stipulated in the alliance, the alliance was between two biotechnology companies, the agreement involved the development of an agricultural or chemical product or a diagnostic product, the alliance was between two firms had a previous alliance, and the lead product was not yet in clinical trials at the time of the alliance. The regressions employ logit specifications. Standard errors are in brackets; odds ratios in parentheses.

	Dependent variable	
	Was agreement renegotiated early?	
Did alliance assign four or more key rights to financing firm?	0.71 [0.46] (2.03)	**0.82 [0.41] (2.27)
Did subsequent years have high growth in equity financing?	-0.23 [0.56] (0.79)	
Growth in biotech equity financing (1995 \$ billions)		
Four or more control rights * Equity financing growth	**0.40 [0.15] (1.49)	0.09 [0.11] (1.09)
Date of the alliance signing	0.11 [0.07] (1.12)	**0.20 [0.09] (1.22)
Age of R&D firm at time of alliance signing	*0.14 [0.08] (1.15)	0.11 [0.07] (1.12)
Was financing firm acquired prior to scheduled alliance end?	***1.85 [0.67] (6.36)	*0.15 [0.08] (1.16)
Was R&D firm acquired prior to scheduled alliance end?	**2.36 [1.15] (10.59)	***1.80 [0.67] (6.05)
Was agreement between biotechnology firms?	0.32 [0.57] (1.38)	**2.35 [1.16] (10.49)
Did agreement focus on agricultural or chemical product?	0.85 [0.93] (2.34)	0.23 [0.57] (1.26)
Did agreement focus on diagnostic product?	1.15 [0.86] (3.16)	0.91 [0.93] (2.48)
Did agreement involve two firms with prior alliance?	-0.17 [0.69] (0.88)	1.08 [0.87] (2.94)
Was lead product not yet in clinical trials at alliance signing?	*0.33 [0.59] (1.39)	-0.13 [0.69] (0.88)
Constant	*-225.90 [138.89]	0.32 [0.59] (1.38)
Pseudo R ²	0.14	-211.25 [138.27]
p-Value of regression	0.002	0.15
Number of observations	160	0.001
		160
		0.203
		137
		0.92 [0.50] (2.51)
		0.03 [0.63] (1.03)
		*0.29 [0.17] (1.34)
		*0.13 [0.08] (1.14)
		**0.20 [0.09] (1.22)
		0.35 [0.66] (1.42)
		0.60 [1.06] (1.82)
		1.25 [0.87] (3.49)
		-0.21 [0.71] (0.81)
		*0.10 [0.60] (1.11)
		*-261.44 [150.24]
		0.08
		0.203
		137

*** Significant at 1% confidence level.

** Significant at 5% confidence level.

* Significant at 10% confidence level.

acquired. The goodness-of-fit and significance of the results are more modest, but the basic pattern holds.

In unreported regressions, we explore the effects of a variety of changes. These include the deletion and addition of other independent variables, the calculation of the change in biotechnology equity issues over a variety of periods (we compute the change using the equity issuance in quarters three through six following the agreement and quarters seven through ten), and the use of different cutoff points to demarcate pro-financing firm agreements. The results remain robust to these changes.

6. Conclusions

This paper takes a first step in empirically examining how shifts in the ability to issue equity affect firm behavior. The biotechnology industry is an attractive setting because of the strong theoretical rationale for financing conditions to affect alliances, the dramatic variation in the ability of all firms in the industry to issue equity, and the high degree of disclosure about project outcomes and transaction structures.

We first demonstrate that biotechnology firms' R&D financing decisions do indeed appear to vary with public market conditions. When public markets are poor, biotechnology firms are at least modestly more likely to finance projects through contract research with pharmaceutical firms. Consistent with theory, contracts signed at times when biotechnology firms raise little external financing assign the most control rights to the financing company. Furthermore, the alliances undertaken during these periods and assigning most of the control to the financing firm perform significantly worse. Evidence regarding the renegotiation of these agreements is broadly consistent with these results.

The analysis suggests two sets of broader questions. First, to what extent is the experience of biotechnology representative? As noted above, the biotechnology industry has certain economic characteristics that make it particularly vulnerable to these kinds of distortions. To what extent are these problems seen in other industries? Second, how do these patterns impact the long-run industry evolution? Numerous policy studies assert that an inability to access equity financing can have distorting effects, particularly in high-technology industries. To cite one recent illustration, the [National Academy of Sciences \(1999\)](#) raises the concern that firms have not been able to finance important innovations in engineering- and physical science-based industries. To what extent can these claims be empirically documented?

Appendix A. Definition of Key Control Rights

Alliances to develop new biotechnologies are complex. Many variants of each control right are found in the alliances. Fully capturing the complexity of these rights in a quantitative analysis is difficult. We describe here the broad control rights that

appear in between 10 and 190 out of the 200 alliances. In this way, we eliminate rights that provide little variation because they are either standardized “boilerplate” and/or exceedingly rare.

The five most important control rights were identified in conversations with practitioners as key to the management of alliances and are described in the text of the paper.

Of the remaining control rights, the first set of control rights addresses alterations to the scope of the alliance. Several alliances provide the funding firm with the right to expand the breadth of the alliance, either by adding to the technologies under development (right #6) or by extending the duration of the project (#7). Nearly all alliances include some provisions for the cancellation of the alliance in particular circumstances (e.g., the bankruptcy or acquisition of one of the parties). In some cases, however, the financing firm has the right to cancel the alliance without cause (#8) or to terminate particular projects (#9). A related cluster of terms addresses the control of the licensed technologies. In some cases, the firm funding the R&D has broad powers to sublicense the technology to other firms (#10) and to continue to sell products developed by the alliance, even after the alliance ends (#11). In many cases, the pharmaceutical company has the right to “shelve” the project, continuing to maintain its exclusive rights even if it decides not to pursue product’s development (#12).

The second cluster of additional control rights relates to intellectual property. Patents and associated scientific knowledge are the most important assets of many biotechnology firms, so it is not surprising that they are the focus of negotiations. The most crucial of these rights relates to the ownership of the patents generated by the project. In some cases, the financing firm owns the patents generated by the alliance (#13). A somewhat weaker right (#14) provides at least partial ownership of these patents: if not restricted by another agreement, a part-owner can freely license a patent to other users. Financing firms often demand control of the patent litigation process (#15).

Other alliance terms relate to “know-how” (unpatented intellectual property). Some alliances stipulate that the financing firm is entitled to transfers of the R&D firm’s know-how (#16). In a few cases, ownership of know-how is assigned to the financing firm (#17). The control of the R&D firm’s scientific publications is also frequently addressed. Many biotechnology firms recruit academic researchers, who are eager to maintain an active publication record. Publications by small biotechnology firms may serve as a favorable signal to the stock market, but premature publications may jeopardize the ability of the parties to obtain patent protection. Consequently, the financing firm may delay publications of the R&D firm (#18) or even suppress them entirely (#19).

The final set of control rights frequently encountered in these alliances covers the governance of the alliance. These alliances typically have one or more oversight boards. While control of the governing board is typically divided evenly between the two firms, occasionally the funding firm is assigned the chairmanship or the tie-breaking vote (#20). The firms funding the R&D have also adopted many of the control rights employed by venture capital organizations while financing small

private firms. These include a seat on the firm's board (#21), as well as an equity stake in the firm, with the associated voting rights (#22). In many cases, instead of receiving common stock, the funding firm receives preferred shares with additional control rights. Among these are the right to participate in future financings of the firm on a *pro rata* basis or anti-dilution provisions, which make it difficult for the R&D-performing firm to sell shares at a lower price (#23). These provisions give the financing firm substantial control over the R&D firm's ability to raise outside financing in the future, and consequently influence the firm's future direction. Registration rights (#24) can be even more onerous to the R&D firm, since they provide a mechanism through which the financing firm can demand that the R&D firm arrange for the sale of its shares in the public market. Such a sale may be very costly or, at times, impossible to arrange. In many cases, the financing firm retains the right to purchase additional shares in the public market (#25). This gives the financing firm the option to acquire the R&D firm, or preserves the threat of such an acquisition.

Appendix B. Definition of Contract Stage

From federal and corporate documents, Recombinant Capital codes the stage of the lead product candidate in the agreement according to a ten-part scheme. These are arranged for the purposes of this analysis approximately in the sequence of the approval process. Discovery research (#1) concerns a research program for which no lead product candidate was identified at the time of the agreement. Lead molecule (#2) concerns a therapeutic discovery program for which a lead product candidate was identified at the time of the agreement, but no animal testing has been undertaken. Pre-clinical (#3) concerns a therapeutic discovery program for which some animal data had been obtained at the time of the agreement signing, but human trials had not yet begun. Formulation (#4) and other pre-clinical (#5) concern research programs not yet at the clinical testing stages that do not involve traditional therapeutic products: formulation refers to the combination of approved or development stage drugs with a vehicle or agent for the administration of such drugs, and other pre-clinical refers to agricultural, diagnostic, or chemical products. (These are ranked after pre-clinical therapeutic discovery programs since the length of time to approval is typically shorter in these cases.) Phase I (#6) concerns a therapeutic development program for which Phase I (safety) human testing was underway at the time of the agreement. It also includes agreements involving agricultural, diagnostic, or chemical development programs for which field or human testing was underway at the time of the agreement. (These tests typically do not have a clearly delineated three-stage structure, as do pharmaceuticals.) Phase II (#7) concerns a therapeutic development program for which Phase II (small-scale efficacy) human testing was underway at the time of the agreement. Phase III (#8) concerns a therapeutic development program for which Phase III (large-scale efficacy) human testing was underway at the time of the agreement. Sometimes firms will undertake joint trials, such as Phase II/III trials. In these cases, the agreement

was coded as being in the more advanced of the two stages. PLA/NDA filed (#9) concerns a research program where testing of the lead product was complete and pending regulatory review at the time of the agreement. Approved (#10) concerns a case where the lead product has already been commercialized at the time of the agreement.

In the tabulations in Table 4, “Discovery” refers to agreements signed at stage #1, “Lead Molecule” to #2, “Pre-Clinical or Formulation” refers to #3, #4, and #5, “Phase I or II” refers to stages #6 or #7, and “Phase III or Under Final Review” refers to #8 and #9. In Table 5, the “Stage of Lead Product at Time of the Alliance” is coded using the ordinal ranking in this appendix.

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