NBER WORKING PAPER SERIES

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Working Paper 7464
http://www.nber.org/papers/w7464

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
January 2000

Mark Edwards made this project possible by allowing generous access to the Recombinant Capital database. Alper Afya, Chris Allen, Tiffany Lin, John Seeg, Evan Wamsley, and Elizabeth Whitburn provided research assistance. We thank George Baker, Paul Gompers, Rebecca Henderson, Tom Hubbard, Robert Merges, Lisa Meulbroek, David Rothman, Scott Stern, Toby Stuart, a number of practitioners, and participants in formal seminars and informal workshops at the American Law and Economics Association annual meetings, Chicago, Harvard, Irvine, the NBER, Northwestern, Toulouse, and UCLA for helpful suggestions. Financial support was provided by the Consortium on Competitiveness and Cooperation, Harvard Business School's Division of Research, and the NBER Project on Industrial Technology and Productivity, with support of the Alfred P. Sloan Foundation. An earlier version of this paper was titled "Financing R&D through Alliances." All errors remain our responsibility. The views expressed herein are those of the authors and not necessarily those of the National Bureau of Economic Research.

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ABSTRACT

While the variability of public equity financing has been long recognized, its impact on firms has attracted little empirical scrutiny. This paper examines one setting where theory suggests that variations in financing conditions should matter, alliances between small R&D firms and major corporations: Aghion and Tirole [1994] suggest that when financial markets are weak, assigning the control rights to the small firm may be sometimes desirable but not feasible. The performance of 200 agreements entered into by biotechnology firms between 1980 and 1995 suggests that financing availability does matter. Consistent with theory, agreements signed during periods with little external equity financing that assign the bulk of the control to the corporate partner are significantly less successful than other alliances. These agreements are also disproportionately likely to be renegotiated if financial market conditions improve.

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1. Introduction

Equity issuance is among the most researched phenomena in corporate finance. The presence of clustering of equity offerings in certain "hot issue" markets has been documented in the academic literature since Hickman [1953]. Yet the implications of shifts in equity financing activity on the operating performance of firms has had little empirical exploration.

The paucity of research may seem initially puzzling. The inability to raise external financing has been highlighted by theoreticians as an important driver of managerial behavior. For example, Froot, Scharfstein, and Stein [1993] argue that the fear of being unable to raise additional financing for value-creating projects leads managers to engage in hedging activities. Another example is Bolton and Scharfstein [1990], who show that when young firms cannot raise capital from the public market, their investors provide fewer incentives than would otherwise be the case (e.g., by committing to refinance the firm, even it is doing relatively poorly). Moreover, numerous policy studies have argued that inability to access equity financing can have distorting effects, particularly in high-technology industries. To cite one recent illustration, the National Academy of Sciences' *Securing America's Industrial Strength* [1999] raised the concern that firms have not been able to finance important innovations in engineering- and physical science-based industries.

At the same time, the lack of attention to these issues is perhaps understandable. With the exception of a few important efforts (Ritter [1984], Bayless and Chaplinsky [1996]), financial economists are still at an early stage in understanding what causes these

shifts in financing availability.[1] Moreover, determining whether the lack of external equity financing is a cause or consequence of a firm's sluggish growth is challenging.

This paper takes an initial step towards exploring the implications of shifts in financing availability. Rather than addressing the impact of financing conditions in a variety of industries and on a range of activities, this paper examines a single arena: technology alliances between smaller biotechnology firms and larger corporations. While this approach must of necessity restrict the generality of the results, it has three advantages.

First, the theoretical literature has some specific predictions as to the effects of financing availability shifts. Aghion and Tirole [1994] argue that in settings where the R&D-performing firm faces capital constraints and does not have the initial bargaining power, an ideal allocation of control rights may not occur. In particular, if it is desirable for the property rights to be transferred to the R&D firm, the best outcome may not be achieved: the financing firm might be willing to transfer ownership, but the R&D firm will not have enough resources to compensate the financing firm. As a result, an inefficient allocation of the property rights occurs, with the financing firm retaining the rights to the invention.

[1]Even the definitions of what constitutes a "hot issue" period varies: for instance, Ibbotson and Jaffe [1975] define this as a period of high initial returns for initial public offerings (IPOs), Choe, Masulis, and Nanda [1993] base their definition on business cycle data, and Bayless and Chaplinsky [1996] consider aggregate issue volume (similar in spirit to the definition used here).

Second, equity financing of biotechnology firms has undergone dramatic variations over the years, as Figure 1 depicts. Moreover, these shifts have been largely in the nature of industry-wide 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 a dramatic effect on all firms' abilities to raise equity. Other shifts were driven by concerns as to how aggressively biotechnology companies would be able to price new drugs. In short, the shifts in the financing environment were dramatic and industry-wide.

Finally, a great deal of information is available about these projects. The bio-engineered compounds that are the subject of these agreements must undergo a rigorous regulatory review process, which enables us to assess the progress of the products being developed. Due to the importance of these agreements as financing sources, almost all important biotechnology alliances are publicly filed. Other factors that may affect the success of the development of new biotechnologies (e.g., the scale and scope of the research effort) can be identified and controlled for.

In the paper, we show that in periods where financing availability was strong, the agreements were more successful, whether measured by the probability that the drug advanced to the next stage in the clinical trials or was approved. We show that the effect was more pronounced in those agreements where the biotechnology company received little of the control, as Aghion and Tirole predict. This helps address concerns that the result is driven by shifts in an unobserved third factor.

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

This paper is related to several strands of the finance literature. A number of works have focused on the reverse of the question discussed here: how firms adjust their performance (*i.e.*, manage earnings) in order to issue equity (such as Teoh, Welch, and Wong [1998]). (Also related are works focusing on the long-run operating performance of firms after offerings, such as Jain and Kini [1994].) Substantially larger bodies of related literature examine how financing constraints affect the investment policies of firms (reviewed in Hubbard [1998]) and the relationship between financial market development and aggregate economic growth (reviewed in Levine [1997]).

This paper is also related to a modest body of empirical research on R&D alliances. Many of the published analyses have focused on the question of which firms enter into alliances (see the overview in Kogut [1988]). A second avenue of research has been examinations of the stock price reaction to the announcements of alliances (e.g., McConnell and Nantell [1985], Chan, *et al.* [1997]). There is a small body of literature on the structure of technology alliances, much of which has focused on the nature of the

payments from licensees to licensors (e.g., Taylor and Silberston [1973], Caves, Crookwell, and Killing [1983], and Hall [1991]).[2]

The organization of the paper is as follows. Section 2 discusses the theoretical rationales for examining the consequences of financial market cycles on technology alliances. 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 set, and the analyses are presented in Section 5. The final section concludes the paper.

2. A Theoretical Framework

Numerous models, beginning with Grossman and Hart [1986] and Hart and Moore [1988] and summarized in Hart [1995], consider incomplete contracting between a principal and an agent.[3] A typical assumption is that it is impossible for the two parties to write a verifiable contract which could be enforced in a court of law and which specifies the effort and final output of the two parties. This is because there are many possible contingencies, all of which cannot be anticipated at the time the contract is drafted. Due to this non-verifiability problem, these models argue that it is optimal for ownership of

[2]In general, the limited empirical attention paid by economists to strategic alliances that fund R&D is striking. These contractual mechanisms are a major source of financing for high-risk projects. For instance, in 1995, the dollar volume of commitments to new alliances in one industry, biotechnology, was almost equal to venture capital disbursements *in all industries* ($3.4 billion vs. $3.7 billion). While obtaining a comprehensive view of alliance financing is exceedingly difficult, tabulations suggest that alliances are the dominant source of external financing for R&D by young firms in many industries, including advanced materials, information technology, and telecommunications (National Science Board [1998]).

[3]This literature, in turn, builds on Klein, Crawford, and Alchian [1978], Williamson [1985], and many earlier works.

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 a 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. (In refinements of the model that will not be discussed here, the authors allow the research unit to instead choose to finance the project through a third party, such as a venture capitalist, and to commercialize the project itself.) 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 may 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 consider two polar cases: when the research unit has the *ex ante* bargaining power, and when the customer does. As we will argue below, bargaining power is likely to vary with the state of the financial markets. 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. In particular, 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.

3. The Biotechnology Industry as a Testing Ground

The Aghion-Tirole model provides the motivation for the empirical analysis of R&D alliances below. In this section, we highlight how the biotechnology industry corresponds in three critical respects with the features of this model. At the same time, it is important to acknowledge that on at least two dimensions, actual alliances involving biotechnology firms pose more complex patterns than the Aghion-Tirole model depicts. Finally, we highlight two empirical predictions from this model.

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, often for human therapeutics but also for agricultural, diagnostic, and veterinary applications. The biotechnology industry has numerous features that resemble the setting depicted in the theoretical literature on incomplete contracts.

First, biotechnology projects—particularly early-stage efforts—are highly complex and uncertain, making it very difficult to specify the features of the product to be developed. As one biotechnology executive relates:

> Redefining the work when the unexpected happens, as it invariably will, [is essential]. Research is by its very nature an iterative process, requiring constant reassessment depending on its findings. If there is a low risk of unexpected findings requiring program reassessment, then it is probably not much of a research program (Sherbloom [1991], pp. 220-221).

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 projects that are not part of the alliance.

Second, the amount of capital raised in the industry has been highly variable. For instance, the equity raised by publicly traded biotechnology firms in follow-on offerings (measured in 1995 dollars) went from $340 million in 1990 to $2.7 billion in 1991, then

fell again to $788 million in 1992. Shane [1995] and Majewski [1998] document that periods with little equity financing activity appear to coincide with investor uncertainty about the fecundity of biotechnology research and/or the industry's commercial prospects. During these periods, the only financing alternatives are corporations and venture capitalists, who presumably can address the information problems that deter other investors, whether through the *ex ante* design of financing mechanisms or the oversight of the firms after the investment.[4] Practitioner accounts suggest that during the periods when there are few public equity issues, the markets are essentially "closed" to biotechnology firms. (Since young biotechnology firms face enormous costs while developing new products, they are typically very aggressive in raising capital.) These accounts suggest that the financing droughts can lead to the bargaining power in alliance negotiations shifting in favor of potential strategic partners. Lawyers specializing in alliance negotiations term these periods "buyer's markets" (Cunningham [1994]).

A third important feature is the degree of disclosure in this industry. Because alliances have been such an important source of financing in the biotechnology industry, much information about alliance structure is disclosed in public securities filings. Furthermore, the progress of drugs through the regulatory process is extensively documented in public filings and private databases. The extent of disclosure in this industry allows us to obtain a comprehensive picture of the success of alliances. This

[4]In addition, young biotechnology firms lack complementary assets such as sales forces and manufacturing know-how, which may take many years to develop. Small, research-intensive firms frequently rely on alliances with larger corporations to avoid having to construct these capabilities, in addition to using them as a source of financing. The focus of this analysis, however, will be on the earlier, pre-commercial phases of biotechnology research.

degree of disclosure can be contrasted with the multi-industry sample of Chan, *et al.* [1997], who note that "firms simply do not announce changes in the status of their alliances following their initial announcements."

Supporting these arguments is the field-based and empirical evidence presented in Lerner and Merges [1998]. They show that the structure of contracts between biotechnology and pharmaceutical firms is consistent with these hypotheses. The assignment of control rights is apparently done in a manner that maximizes innovative output, except in cases where the R&D firm has few resources and little external financing is available. In these instances, the R&D firm is assigned significantly fewer control rights than might be expected otherwise.

At the same time, biotechnology alliances present a more complex picture than many incomplete contracting models. We will highlight two of these concerns here, and the manner in which we at least partially address them.

First, the basic Aghion-Tirole model presents a setting where the parties bargain over a very reduced set of parameters. As they relate:

> the contract only specifies the allocation of the *property right* on any forthcoming innovation, a *sharing rule* on the verifiable revenue (license fee) obtained by the research unit, and any *verifiable* amount of *customer investment* (Aghion and Tirole [1994], p. 1189 (emphasis in original)).[5]

[5]The authors also discuss how if there are multiple innovations, the ownership of individual innovations may be assigned differently, with the each party getting property rights to the innovations where it has a comparative advantage in creating value.

By way of contrast, actual alliances are complex documents, often extending for 100 pages or more and assigning a wide variety of control rights. Rather than a single right, control rights over various aspects of the alliance are treated differently. For instance, while ownership of the patents may be assigned to the R&D firm, the financing firm may be given the right to control any litigation involving these patents and to access the know-how generated by the alliance. Practitioners suggest that no single control right stands out as critical. Rather it is the accumulation of rights to control contingencies that makes an alliance particularly favorable to the R&D or the financing firm. Thus, it is important to examine the allocation of control rights as a whole, rather than any single right.

Second, the Aghion-Tirole model assumes a one-time contracting process between the two parties. Actual alliances reveal more complex contracting patterns than the "one-shot" contracts depicted in this paper. For instance, pairs of firms undertake repeated sets of alliances on different topics. Pharmaceutical firms and large biotechnology firms also make equity investments in small biotechnology concerns, often in the hopes of ultimately signing alliances with these concerns. These prior interactions may lead to increased trust between the two parties and fewer concerns about the R&D firm providing diminished effort. To address this concern at least partially, we control for alliance pairs where the firms have a prior contractual relationship.

While acknowledging these limitations, it appears the biotechnology industry is in many respects a natural testing ground. In particular, we will examine two questions:

- *Whether success rates differ in agreements that are (i) signed in periods with little external equity financing availability and (ii) cede the bulk of the control to the financing firm.* When no external equity financing is available, biotechnology firms

are likely to have little bargaining power. As argued above, theory suggests that they will be less likely to complete agreements that maximize innovative output during these periods: in particular, they will in some instances cede control when innovative output would have been maximized had they retained it.

- *Whether the less attractive agreements are renegotiated.* The availability of financing to biotechnology firms has undergone dramatic changes. 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 to be the ones are disproportionately renegotiated.

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 either more successful (*e.g.*, if the greater ability of firms to raise equity financing reflects the fact that there are many attractive opportunities to exploit) or less so (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.

4. The Data Set

A. Identifying the Contracts

This paper is based on a database of alliances compiled by Recombinant Capital, a San Francisco-based consulting firm specializing since 1988 in tracking the biotechnology industry. Publicly traded biotechnology firms, like other concerns, are required by the U.S. 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 fact that biotechnology firms typically derive little income from sales and payments as part of alliances represent a large share of their total revenues. This interpretation about what must be filed with the SEC also appears to reflect industry practice. In contrast, publicly traded multimedia developers also often have very little revenue outside of alliance payments, but rarely file their agreements with media companies.

Biotechnology alliances are typically filed as amendments to 10-K, 10-Q, S-1, or 8-K statements. In addition, a number of state governments require privately held companies with employee stock option plans to file material documents, which they make available to the public. These are also collected and coded by Recombinant Capital.

As of December 1998, Recombinant Capital had identified over 7000 biotechnology alliances by examining SEC filings, news accounts, and press releases. By this date, Recombinant Capital had analyzed about 900 of the approximately 4800 alliances that had been filed with the SEC or other government bodies. When performing analyses, Recombinant Capital seeks to ascertain any information deleted from the filed alliances by examining subsequent filings by the firms, which sometimes reveal royalty rates or lump-sum payments redacted in the original agreements.[6] The Recombinant Capital database is typically licensed by major pharmaceutical, accounting, and law firms

[6]Firms can request confidential treatment for the key information in these alliances. Their failure to disclose this information, however, may become an issue if the firm is sued for security law violations. Shareholder class-action litigation has occurred frequently in high-technology industries.

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

For our analysis, we selected a random sample of 200 of the analyzed alliances to encode. We sought to create a population that avoided undesirable heterogeneity. In particular, we eliminated alliances where:

- One of the parties was a university, medical center, other non-profit organization, or government agency.
- One of the parties had 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 had a previous alliance covering the same set of technologies, and consequently were renegotiating the terms of an earlier alliance.
- There was neither a research nor a product development component, but the alliance simply involved the marketing of an existing product.
- More than two firms were involved, making the analysis of the contract less tractable.
- The agreement as filed contained neither information on the duration of the alliance nor the structure of the payments between the two firms.
- The agreement was signed after 1995, so that it was difficult to analyze alliance outcomes.

Table 1 compares the alliances in the sample with the universe of filed agreements, as well as the subset summarized by Recombinant Capital. The table highlights the fact that our criteria disproportionately eliminated several classes of agreements. The Recombinant Capital database included a variety of contracts, such as licenses of approved products and diagnostic kits, that did not meet the definitions above, particularly the requirement that there be a research or product development element. The observations in the sample were concentrated towards the end of the sample. This

reflected 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 interest to its clients.

Recombinant Capital summarized the alliances according to a systematic approach developed by Mark Edwards, the firm's managing director. Using the summary in the Recombinant Capital database, we coded several measures. The first of these was the number of control rights assigned to the financing firm (out of a total of 25, which are listed in Appendix A). In each case, a value of one indicated that the particular right was allocated to the financing firm, and zero if not. This structure for the analysis was suggested by the legal treatment of technology licenses, which reserves for the licensor any rights not explicitly granted to the licensee (Merges [1995]). We also wished to control for the scale of alliance. We thus also computed the sum of all pre-commercial payments that the financing firm committed to make as part of the alliance (some of these may have been contingent on the achievement of technological or regulatory milestones), the amount that the financing firm provided up-front at the signing of the alliance, and the minimum duration of the alliance.

B. Supplemental Information

For each of the 200 alliances, we gathered a variety of supplemental data. First, we determined from the Recombinant Capital database the nature of the regulatory review facing the technology being developed. The review of new human therapeutics by the U.S. Food and Drug Administration (FDA) is frequently exhaustive, often

stretching for a decade or longer. Agricultural and veterinary bio-engineered products face somewhat less arduous reviews, as do diagnostic products.

Second, we identified the progress of the lead product under development at the time of the agreement. The Recombinant Capital database identified—and we corroborated 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.) This information was determined by Recombinant Capital from federal and corporate documents.

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

Fourth, knowledge spillovers from other R&D projects may have an important impact on the success of an R&D project. (Henderson and Cockburn [1996] provide evidence to this effect from the pharmaceutical industry.) We thus compiled the overall research spending of the contracting firms. We determined this data from the Compustat and Worldscope databases for the end of the fiscal year immediately prior to the alliance.

For firms where this information was not available from Compustat or Worldscope, we gathered 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 employed a variety of information sources. For a number of years, Recombinant Capital offered discounts on its products to individuals who provided it with documentation about the evolution and outcome of alliances in its database. As a result, the consulting firm compiled a large number of press releases and securities filings about alliances. In addition, the organization compiled a database of all pharmaceutical products under development by biotechnology firms. We also searched SEC filings and news stories in the LEXIS-NEXIS and Dow-Jones News Service databases. Finally, we used two specialized databases that tracked the development of pharmaceutical and bio-engineered products through monthly surveys of biotechnology and pharmaceutical firms, as well as reviews of FDA filings: IMS and PharmaProjects. While these databases had some limitations—in particular, firms may not always have disclosed strategically important pre-clinical projects—industry executives believed that they gave a fairly comprehensive picture of drugs in the clinical stages of development.

Finally, we determined whether the alliance was renegotiated. We found this information from the Recombinant Capital database (which noted such renegotiations in its alliance summaries and compiled press releases announcing renegotiations), SEC filings, and press accounts in LEXIS-NEXIS and Dow Jones News Service databases.[7]

[7]We also computed the inflation-adjusted amount of equity financing raised by biotechnology firms in public offerings in the four quarters prior to the quarter of the

Table 2 summarizes the characteristics of the alliances, as well as those of the firms entering into these alliances. Several patterns can be observed from these summary statistics. Most alliances were 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 was substantial, with the average financing firm having several hundred times the revenues and assets of the mean R&D firm. The financial position of the typical R&D firm was precarious, with negative net income and operating cash flow. In fact, the mean R&D firm's operating cash flow was sufficiently negative that it would exhaust its cash and equivalents in about three years' time (if the losses continued at the same level and no additional financing was received). The mean alliance entailed a minimum period of just less than four years before the financing firm could terminate funding. The median was three years, which reflected the skewness of the distribution, with a few alliances being considerably longer than the others. The typical alliance called for the financing firm to make total pre-commercialization payments of $29 million. Only $1.8 million, however, was provided on average up-front, and many of the subsequent payments were contingent on the achievement of technological or regulatory milestones. The assignment of control rights to the financing firm was highly variable, with between zero and 16 such rights (out of a possible 25) assigned.

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offering, using data from Recombinant Capital's financing database and a wide variety of other publications, as described in Lerner [1994].

5. Empirical Analyses

In this section, we proceed in three parts. We first examine the relationship between financing conditions, transaction structures, and alliance outcomes in univariate comparisons. We then undertake regression analyses. We finally explore the pattern of renegotiation of the alliances.

A. Relationship Between Control Rights and Alliance Outcomes

Table 3 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.[8] Observations are divided by their status at the time the agreement was signed. Note that the time that the products have 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.[9]

The table highlights the fact that relatively few products had been approved by the end of 1998. In all, 14% of the alliances have resulted in an approved drug (26% of those

[8]A complication in this analysis, as well as that reported in Table 4, was introduced by agricultural, diagnostic, and veterinary projects where there was not a clear stage of the regulatory review process corresponding to Phase III for therapeutic products. In these instances, we examined only whether the project entered the regulatory review process and whether the project was approved. Another complication was the modest number of cases where the lead product was abandoned or de-emphasized in favor of another product that surpassed the lead product in the regulatory review process. In these cases, we tracked the status of the most advanced product covered by the alliance.

[9]In a number of cases, the agreements between the R&D and financing firm had been terminated by the end of 1998. While in most cases, work on the lead molecule ended after the agreement lapsed, in some instances the biotechnology company funded further development itself or found another corporate partner. The termination of alliances developing ultimately successful projects often was a consequence of a corporate merger or shift in strategy. Because of these instances, we measured the ultimate success of the project, rather than the duration of the alliance itself.

that were in Phase I or Phase II trials at the time the alliance was signed). This low success rate was consistent with evidence about the success of pharmaceuticals more generally: for instance, the Pharmaceutical Research and Manufacturers of America [1998, Figure 3-1] estimated that for every five drugs that entered Phase I clinical trials in recent years, only one was ultimately approved for sale by the FDA.

We then examined whether the theoretical suggestions regarding alliance success were borne out in the data. To do this, we compared the relationship between assignment of control and success in agreements signed during periods with and without substantial external equity financing by biotechnology firms. We compared four measures of success in transactions that were favorable to the R&D firm (which assigned less than seven rights to the financing firm out of a possible twenty-five) and in all other agreements. We contrasted these differences in alliances signed in periods where the level of external equity financing in constant dollars in the previous four quarters was above the median and those where it was equal to or below the median.

The results, reported in Panels B and C, suggest that alliances in which the fewest control rights were assigned to the financing firm had the greatest success. The differences were substantial in the cases where the agreement was signed in a poor market. The differences in these four cases averaged 25.9% and were statistically significant at the five percent level in two cases and at or near the ten percent level in the other two cases. In the case of the agreements signed in favorable markets, the

differences were smaller in magnitude, averaging 17.1%. The effects were only significant when we used the measure of whether a product was approved.[10]

While these tabulations may be interpreted as providing some support for the hypotheses in Aghion-Tirole [1994], our interpretation of them must be very cautious. For instance, these comparisons may be misleading due to the different "vintages" of the projects. Consider the possibility that the allocation of control rights in alliances changed over time. A disproportionate number of older alliances, in which the lead product had more time to progress through regulatory reviews, may have assigned few control rights to the financing firms. Clearly, this and other effects can only be addressed through regression analyses.

B. Regression Analyses

In addition to concerns about the differences in alliance "vintage," a variety of other factors may affect the success of bio-engineered products. This paper sought to address a variety of concerns:

- As noted above, the review process of agricultural, diagnostic, and veterinary products is frequently less rigorous.
- The probability of ultimate approval, as Table 3 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 was important.

[10]In a variety of unreported tabulations, we explored the robustness of the results to the use of different cut-off points. The magnitude of the differences between the effects in favorable and unfavorable markets appeared to strengthen when we used either more or less permissive definitions of what constituted a favorable market. When we changed the definition of "pro-R&D firm" agreements to include significantly more agreements in this categorization, however, the differences weakened. This was true both for the differences between the more and less favorable agreements in terms of the allocation of control and the differences in differences.

- 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 [Arrow, 1962]—that economies of scale and scope play an important role in the determining the success of pharmaceutical R&D projects. We employed two control variables in the reported regressions: the total amount that the financing firm committed to the alliance, as well as the overall R&D expenditures of the R&D firm.

Table 4 presents six regression analyses. In each case, we hypothesized that new biotechnology products were generated through a production function, $Y = F(x,\beta)$, where Y was the probability that a given product is developed, x was a vector of inputs or attributes that influence the discovery process, and β was a vector of coefficients. Since our observations consisted of the time until a given product commenced trials or was approved, we used a parametric survival model.

We employed a Cox proportional hazard specification, in which we estimated the probability that a given event occurred over time. Essentially, the Cox model estimates a hazard function, h(t), for an event occurring at any given time t, where $h(t)=H_0(t)e^{\beta_1 x_1+\beta_2 x_2+ \ldots+\beta_N x_N}$. The first through fourth regressions estimated the time until the approval of the product. Observations were right-censored at the end of 1998: no data was used after this point. The fifth and sixth regressions analyzed the time until the next major milestone in the approval process. This was defined as the commencement of clinical or field trials for products that were not yet in trials at the time the alliance was signed, the commencement of Phase III trials for therapeutics that were in Phase I and II

trials, and regulatory approval for therapeutic products in Phase III trials or whose final application was pending and for agricultural, diagnostic, and veterinary products in trials.

Not surprisingly, in each of the regressions, projects that were in later stages of development were more likely to progress to the next stage. In the two regressions analyzing whether the project reached the next stage in the approval process, alliances in which there was a larger funding commitment by the financing firm were also associated with greater success, consistent with earlier results about the importance of scale in research projects. Finally, alliances signed in periods where more equity was being raised by biotechnology firms were more likely to lead to approved projects (though the coefficients were insignificant in the analyses of whether the development project reached the next stage of the approval process).

The coefficients of the interaction terms were consistent with the predictions of Aghion and Tirole [1994]. As noted above, strong equity financing markets were associated with greater project success. When many control rights were assigned to the financing firm, the effect of strong financing markets was even more positive. Put another way, instances where there were weak financing markets and few control rights allocated to the financing firm were associated with particularly poor performance. The results were robust to using either the dollar volume of financing activity or dummy variables denoting little activity, measuring financings in the last one and four quarters, and employing the count of control rights assigned to the financing firm as well as dummy variables with different cut-off points. The effects were significant not only statistically (at between the one and ten percent confidence levels) but also economically.

For instance, in the leftmost regression, a ten percent increase in external financing activity when six control rights were assigned to the financing firm (and all other dependent variables are at their means) increased the hazard rate by 43%. When twelve control rights were assigned to the financing firm, the rate increased by 69%.

The Cox specification constrained the probability that an event occured at any given time to be proportional. If the probability that a drug was approved was twice as high in one group than in another, the model assumed that this was the case one, two, or five years after the alliance signing. We examined this assumption of proportional hazards, both jointly for all variables and for the individual independent variables. In no case in Table 4 did we reject the proportional hazard assumption at the five percent confidence level in the joint test, or at the ten percent level for the test of the interaction term. We did, however, reject the proportional hazard assumption at the ten percent confidence level for two independent variables.[11]

One concern with these regressions related to the measure of the dollar commitment by the financing firm. It may be that alliances that were completed in stronger financing markets or where more control rights were allocated to the R&D firm also were ones in which the financing firms made firmer financial commitments. The

[11]As a robustness check, we re-estimated these equations using stratified Cox regression estimates, where we divided the observations into groups on the basis of the variables whose hazard rate appeared 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 was allowed to have a different hazard rate. While in some cases, the coefficients of other variables varied across equations, the differences across groups in the coefficient of the interaction variable were minimal.

scale of these R&D projects in these cases may have been larger, even after controlling for the stated amount of pre-commercialization payments.[12]

To address this possibility, we examined two other alliance characteristics, 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. These were likely to be correlated with the extent of funding for the alliance: longer alliances and ones with larger payments up-front may have been 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 was due to their greater scale, these alternative measures should also have considerable explanatory power. In unreported regressions, we added dummy variables for agreements of differing lengths and similarly controlled for the size of the up-front payment. The variables were almost uniformly insignificant and variable in sign, while the interaction term was little changed. Thus, it did not appear that the results were due to variations in alliance scale.

In unreported regressions, we explored the sensitivity of the results to a variety of changes in the specification. First, we employed another measure of control rights. In particular, we implicitly assumed above that each of the 25 control rights was equally important. We repeated the analyses, employing only the five control rights identified as the most critical during conversations with practitioners (denoted as Rights #1-#5 in

[12]This might have been a consequence of the measuring the pre-commercialization payments with error. In particular, some of the contingent milestone payments included in the total may have been conditional on remote contingencies and consequently had a low expected value.

Appendix A). The results were similar to those reported above. Second, we included the R&D expenditures of the larger firm as an additional control for the scope of the project. While this reduced the sample size—many foreign financing firms did not report R&D expenditures—the results were qualitatively similar. Finally, we also tested whether the results were robust to addition of a number of variables. We added dummy variables to denote cases in which the financing firm had made a prior equity investment into the R&D firm, the location of the firm (to control for the geographic effects identified by Zucker, Darby, and Brewer [1998]), and the disease targeted by the therapeutic alliances. We added 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 were little changed.

C. Alliance Structure and Renegotiation

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

One implication of this view related to the renegotiation of alliances. Agreements where the optimal division of control rights could not be achieved should have been more frequently renegotiated if conditions changed. This suggested an empirical test based on the overall financing environment for biotechnology firms, which, as suggested above,

was subject to dramatic changes. We examined whether the agreements were renegotiated prior to the minimum time stipulated in the agreement. We hypothesized that pro-pharmaceutical company agreements would be more likely to be renegotiated during periods where the external financing environment for biotechnology firms improved considerably, which was likely to be associated with a shift in bargaining power.

Table 5 presents two regression analyses of the likelihood of premature renegotiation. (Only agreements whose scheduled completion date was prior to January 1, 1999 were included in the regressions, leading to a slightly smaller sample size.) The dependent variable was a dummy that took on the value one if the alliance was renegotiated prior to its scheduled completion date. The first regression employed as independent variables dummies that denoted the quartile of agreements with the fewest control rights assigned to financing firm, the quartile of agreements with the most dramatic improvement in the financial markets after the agreement (defined as the difference between the inflation-adjusted dollar volume of equity offerings by biotechnology firms in the fifth through eight quarters after the alliance signing and the four quarters prior to the alliance signing), the interaction between these variables, and a variety of controls. In the OLS regression reported in the first column, the interaction term was significantly negative: during periods of increased financing activity, pro-R&D company agreements were less likely to be renegotiated. One way to express the magnitude of this effect was to consider the predicted probability of renegotiation during a period when there was a dramatic increase of external financing (keeping all other

independent variables at their means). For pro-R&D firm agreements, the predicted probability was virtually zero; for all other agreements, it was over one-half.

Because in no cases where the interaction term was equal to one were renegotiated, we could not report the results of a logit regression in this case. We could, however, if we expressed the external equity financing raised (and the interaction term) as continuous variables. This regression is reported in the second column of Table 9. Once again, the interaction term was significantly negative. We explored the effects of a variety of changes, such as the deletion and addition of other independent variables, the calculation of the change in biotechnology equity issues over a variety of periods, and the use of different cut-off points to demarcate pro-R&D firm agreements. The results remained robust to these changes.

5. Conclusions

This paper takes a first step in examining how shifts in the ability to issue equity affects firm behavior. It examines 200 R&D alliances involving biotechnology firms. This is an attractive empirical setting because of the strong theoretical rationale for financing conditions to matter here, 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. Consistent with theory, contracts that are signed at times when biotechnology firms are raising little external financing and that assign the most control rights to the large corporation 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, how pervasive shifts in financing availability have been? While the variation in aggregate equity issuance volume has been well documented, what have been the patterns at the industry level? To what extent does the more general historical record support the claims that inter-industry variations in equity issuance are driven by the information-based explanations hypothesized by Shane and Majewski (as opposed to, for instance, relative valuation levels, as argued by Pagano, Panetta, and Zingales [1998])? Second, how have these patterns impacted emerging industries, particularly those with substantial financing needs and large information asymmetries? To what extent can deleterious consequences—as claimed by National Academy of Sciences and Council on Competitiveness studies—be empirically documented?

Perhaps nowhere is this question illustrated more sharply than in the U.S. venture capital industry, which has sharply focused on information technology and healthcare investments (representing over 80% of total financing). Meanwhile, venture investors have virtually ignored many classes of technologies with substantial innovative activities (see the tabulations of venture disbursements and patenting in Kortum and Lerner [1998]). To what extent are these patterns—and the even more dramatic concentration in certain subsets of information technology, such as electronic commerce—reasonable responses to investment opportunities? Are otherwise viable industries stunted by the concentration of these funds? The determinants and consequences of shifts in equity financing availability are rewarding topics for future research.

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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 focus in this paper, as in Lerner and Merges [1998], on 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. 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 may believe 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. Retaining rights to undertake initial manufacturing may be more important to the party who has more manufacturing expertise.

3. Control of manufacturing after product approval. This is a particularly significant right for human therapeutic products. When the 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.

The final two key control rights relate to the marketing of the bio-engineered product. Almost all pharmaceutical firms have large sales forces, which engage in the time-consuming process of developing personal relationships with doctors and hospital administrators. At least until very recently, most biotechnology firms have sought to develop similar capabilities. These firms believed that a sales force would allow them to increase their profit margins and that this sales force would gather strategically important information. These were:

4. Creation of exclusive territory for R&D firm. The presence of this control right would grant exclusive rights to the R&D firm to market the product in one or more markets defined by geography (country) or product type (disease indication).

5. Creation of co-marketing rights for R&D firm. The presence of this control right would allow the R&D firm to participate in the marketing of the product in one or more markets.

The second 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 sub-license 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 third cluster of 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 outright (#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 began. 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 veterinary 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 veterinary 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 3, "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 4, the "Stage of Lead Product at Time of the Alliance" is coded using the ordinal ranking in this appendix.

Table 1—Characteristics of all filed agreements, those summarized by Recombinant Capital, and those included in the sample. Each column indicates the year and stage at the time the agreement was signed and the primary focus for a different set of agreements. The first column indicates the distribution of all alliances, licensing arrangements, and asset sales involving biotechnology companies between 1980 and 1995 filed with the U.S. Securities and Exchange Commission or state regulatory bodies who make such information public. The second column indicates the distribution of all such agreements summarized by Recombinant Capital. The final column characterizes the final sample of 200 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980-1995 period.

	All Filed Agreements	*All Summarized Agreements*	*Final Sample*
Time Period:			
1980-1987	20%	11%	14%
1988-1990	18	21	21
1991-1992	26	26	34
1993-1995	36	42	31
Stage of Product at Signing:			
Discovery/Lead Molecule	65	57	64
Pre-Clinical Development	9	11	21
Undergoing Regulatory Review	17	23	15
Approved for Sale[a]	9	9	0
Primary Focus of Agreement:			
Human Therapeutics	75	83	92
Human Diagnostics[b]	18	15	4
Agricultural or Veterinary Applications	6	2	4

[a]The sample is constructed to include only alliances with a research or a product development component. Thus, many of the agreements in the database involving approved products, which solely entail the marketing or sale of an existing product or process, are excluded from the sample.

[b]Many of the agreements involving human diagnostics entail the marketing or sale of an existing product or process developed by a biotechnology company in the course of a program to introduce a new therapeutic. (Because diagnostics tests are frequently of modest economic importance and viewed as tangential to the firm's product development focus, biotechnology firms often sell these outright to major firms specializing in this area.) Because these agreements are not alliances with a research or product development component, they are excluded from the sample.

Table 2—Characteristics of the sample. The sample consists of 200 technology alliances initiated between biotechnology and pharmaceutical companies or between biotechnology firms in the 1980-1995 period. The table summarizes the financial market conditions around the time of the alliance and the characteristics of the firms in the alliance and the alliance itself. The stage of product, focus of alliance, and characteristics of pair of firms in alliance measures are all dummy variables. The financial condition 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*
Stage of Lead Product at Time of Alliance:					
Discovery/Lead Molecule	0.64			0	1
Pre-Clinical Development	0.21			0	1
Undergoing Regulatory Review	0.15			0	1
Focus of Alliance:					
Human Therapeutics	0.92			0	1
Human Diagnostics	0.04			0	1
Agricultural or Veterinary Applications	0.04			0	1
Condition of Financing Firm:					
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
Condition of R&D Firm:					
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
Characteristics of the Alliance					
Date of Alliance	Jun. 1991	Dec. 1991	3.1 years	Jan. 1980	Dec. 1995
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 R&D Firm (out of 25)	9.22	9	2.68	0	16

Table 3—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. 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, veterinary, 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, veterinary, or diagnostic products are excluded from the "At Least in Phase III Trials" tabulation. Panels B and C report the difference between the percentage of agreements reaching each stage for alliances where six or fewer control rights assigned to the financing firm (out of a total of 25) and seven or more 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 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 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 veterinary products undergoing trials) are coded in the affirmative.

Panel A: Summary of Entire Sample

	Status in December 1998			
Status at Time of Signing	*Not Yet In Trials*	*At Least in Phase I Trials*	*At Least in Phase III Trials*	*Approved*
Discovery	69%	31%	12%	5%
Lead Molecule	38	62	10	10
Pre-Clinical or Formulation	26	74	33	19
Phase I or II			65	26
Phase III or Under Final Review				71
All Transactions	51	49	27	14

Panel B: Agreements Signed in Unfavorable Financing Markets

	Status in December 1998			
	At Least in Phase I Trials	*At Least in Phase III Trials*	*Approved*	*At Least One Step Further*
Difference, "pro R&D firm" alliances and others	25.5%	29.6%	25.2%	23.1%
χ^2-statistic from test of difference	2.57	4.85	5.46	3.22
p-Value, χ^2 test	0.109	0.028	0.019	0.073

Panel C: Agreements Signed in Favorable Financing Markets

	Status in December 1998			
	At Least in Phase I Trials	*At Least in Phase III Trials*	*Approved*	*At Least One Step Further*
Difference, "pro R&D firm" alliances and others	11.5%	11.9%	30.0%	15.0%
χ^2-statistic from test of difference	0.49	0.84	14.91	0.96
p-Value, χ^2 test	0.483	0.360	0.000	0.327

Table 4—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 through fourth regressions is the date at which the lead product in the alliance was approved. In the fifth and sixth regressions, the dependent variable is the date when 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 veterinary products undergoing trials). The independent variables are dummy variables denoting whether the agreement entails the development of an agricultural or veterinary 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, the total R&D spending of the R&D firm in the year prior to the alliance, and various variables denoting whether the agreement was signed in periods with little equity financing by biotechnology firms and involved the assignment of many control rights to the financing firm. All financial measures are in 1995 dollars. Standard errors in brackets.

	Dependent Variable:					
	Date of Lead Product Approval				*Date of Entering Next Phase*	
Did agreement focus on agricultural or veterinary product?	1.02 [0.78]	*1.30 [0.73]	0.74 [0.80]	0.65 [0.80]	***1.20 [045]	***1.28 [0.46]
Did agreement focus on diagnostic product?	0.90 [0.76]	0.92 [0.80]	0.80 [0.79]	0.79 [0.76]	0.45 [0.53]	0.51 [0.53]
Stage of lead product at time of alliance	***0.37 [0.09]	***0.41 [0.09]	***0.38 [0.09]	***0.35 [0.09]	***0.20 [0.04]	***0.20 [0.04]
Did agreement involve two firms with prior alliance?	1.25 [0.78]	*1.32 [0.74]	1.03 [0.81]	0.94 [0.83]	-0.08 [0.44]	-0.08 [0.44]
Total pre-commercialization payments in the alliance ($ millions)	0.007 [0.007]	0.009 [0.007]	0.008 [0.006]	0.008 [0.006]	**0.007 [0.003]	**0.007 [0.003]
Total R&D spending by R&D firm in prior year ($ millions)	-0.01 [0.02]	-0.01 [0.02]	-0.01 [0.02]	-0.01 [0.02]	-0.01 [0.01]	-0.01 [0.01]
Volume of equity financing in previous four quarters ($ billions)	**1.30 [0.64]				0.10 [0.09]	
Was equity financing in previous four quarters below median?		*-1.43 [0.84]				
Volume of equity financing in previous quarter ($ billions)			**3.68 [1.54]	***10.05 [3.72]		
Was equity financing in the previous quarter below median?						-0.39 [0.25]
Count of control rights assigned to financing firm	-0.03 [0.11]			0.02 [0.11]		
Did alliance assign seven or more rights to financing firm?		***-2.59 [0.91]	-0.11 [0.61]			
Did alliance assign twelve or more rights to financing firm?					0.66 [0.41]	*-0.79 [0.44]
Interaction between financing and control variables	*0.18 [0.09]	**-2.10 [1.05]	**4.63 [1.83]	***1.37 [0.53]	*0.37 [0.20]	***-1.67 [0.59]
Log likelihood	-86.46	-87.28	-85.66	-83.94	-421.36	-418.99
χ^2-statistic	39.81	38.17	41.40	44.84	31.22	35.96
p-Value of χ^2-statistic	0.000	0.000	0.000	0.000	0.000	0.000
Number of observations	171	171	171	171	171	171

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

Table 5—Regression analyses of the premature renegotiation of R&D alliances. The sample 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 prior to the end of 1998. 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 six or fewer control rights to the financing firm (out of a total of 25), 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 in the top quartile or the dollar volume (in billions of 1995 dollars) of this difference, an interaction between the control rights dummy 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 biotechnology companies, the agreement involved the development of an agricultural or veterinary product or the development of a diagnostic product, the two firms had a previous alliance, and the lead product was not yet in clinical trials at the time of the alliance. The first regression employs an ordinary least squares specification; the second, a logit specification. Standard errors in brackets.

Independent Variable	Dependent Variable Was Agreement Renegotiated Early?	
Did alliance assign six or fewer rights to financing firm?	-0.002 [0.12]	- 0.72 [0.60]
Did subsequent years have high growth in equity financing?	0.05 [0.10]	
Growth in equity financing		0.06 [0.10]
Six or fewer control rights * Equity financing growth variable	**-0.52 [0.25]	**-0.73 [0.35]
Date of the alliance signing	0.02 [0.01]	0.09 [0.07]
Age of R&D firm at time of alliance signing	**0.02 [0.01]	*0.14 [0.07]
Was financing firm acquired prior to scheduled alliance end?	***0.41 [0.13]	***1.85 [0.66]
Was R&D firm acquired prior to scheduled alliance end?	**0.46 [0.18]	**2.51 [1.14]
Was agreement between biotechnology firms?	0.06 [0.11]	0.33 [0.56]
Did agreement focus on agricultural or veterinary product?	0.29 [0.19]	1.43 [0.89]
Did agreement focus on diagnostic product?	0.13 [0.19]	0.47 [0.99]
Did agreement involve two firms with prior alliance?	0.004 [0.14]	0.01 [0.72]
Was lead product not yet in clinical trials at alliance signing?	0.07 [0.12]	0.33 [0.59]
Constant	-38.86 [26.50]	-173.68 [136.58]
Log likelihood		-91.28
Adjusted R^2 or Pseudo R^2	0.12	0.14
F-statistic	2.83	
χ^2-statistic		30.13
p-Value	0.001	0.003
Number of observations	160	160

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

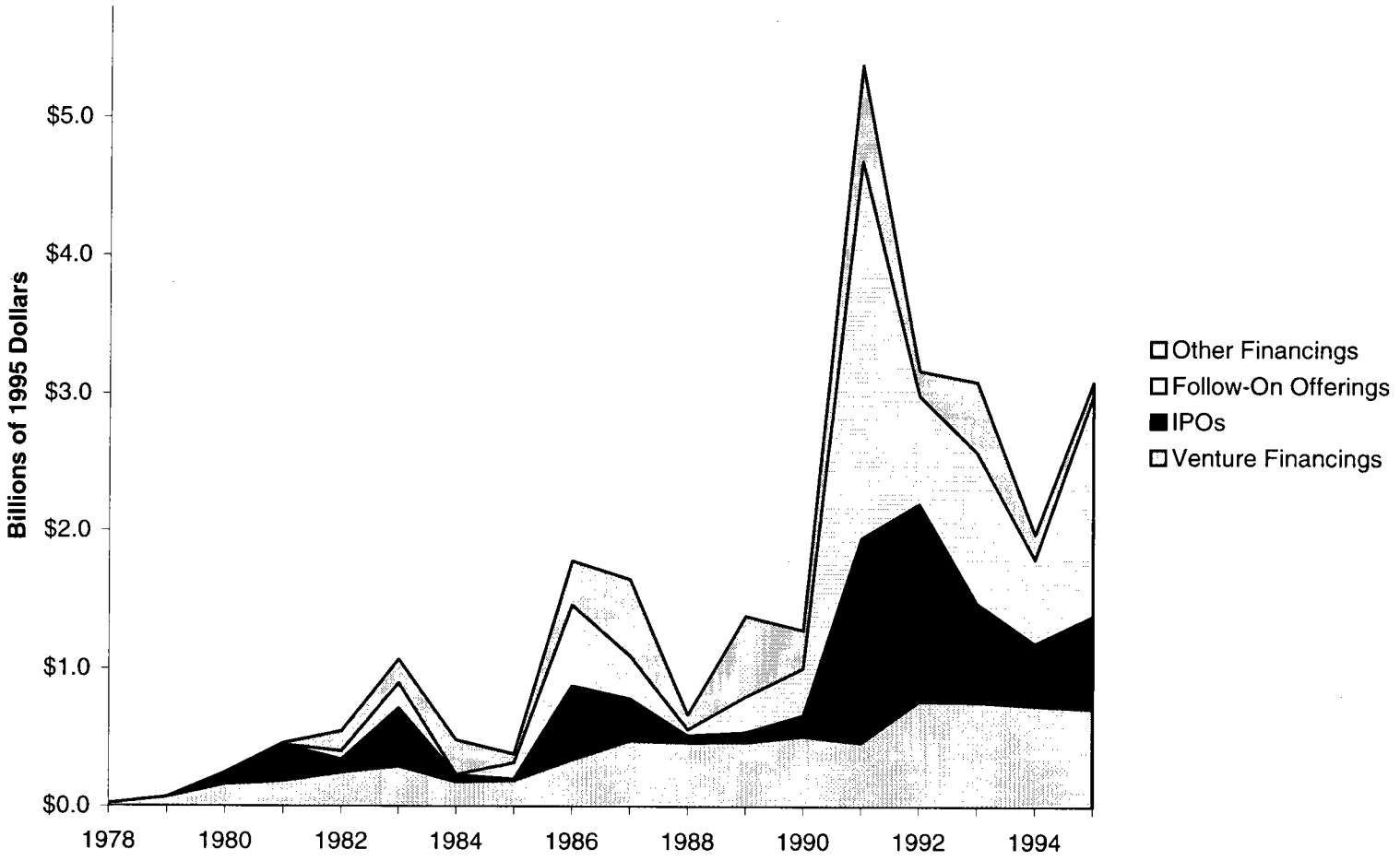

Figure 1—External financing of the U.S. biotechnology industry. The chart depicts the amount raised by U.S. new biotechnology firms through private venture financings, initial public offerings, follow-on public equity offerings, and other financing sources. (Alliance-related financings are excluded.)