The Impacts of the Rise of Paragraph IV Challenges on Startup Alliance Formation and Firm Value in the Pharmaceutical Industry

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Abstract:

Court decisions in 1998 encouraged generic producers to pursue Paragraph IV patent challenges. A follow-up decision in 2000 marked the first successful challenge involving a blockbuster and brought further attention to this pathway for generic entry. We consider the impacts of these decisions on R&D-based startups, and we focus on the propensity to form alliances as a primary channel of impact. We find substantial negative impacts on alliance formation and firm value, and only the first event's impacts are restricted to small molecules. The results suggest that policy analyses in settings with R&D-based startups should consider impacts on alliance formation.

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Solow (1957) established that innovation is the primary source of long-run economic growth. The contribution of innovation to welfare is perhaps most important in the area of health, and Murphy and Topel (2003, 2006) estimate that enormous welfare gains could result from even incremental improvements in the rate of discovery of medical innovations. Given this, it is important to conduct thorough assessments of policies that impact the generation and diffusion of medical innovations.

This paper focuses on intellectual property rights (IPR) policies in the pharmaceutical industry - a key source of medical innovations. Nordhaus (1969) describes how optimal policies must strike a balance between innovation and diffusion: weakening IPR reduces innovation, while strengthening IPR reduces the diffusion of existing products and processes. Judicial decisions in 1998 and 2000 (described in detail in the next section) affected the balance between innovation and diffusion by encouraging generic producers to pursue "Paragraph IV" patent challenges against innovators. We analyze the impacts of these policy changes on R&D-based startups, and we focus on the propensity to form alliances as a primary channel of impact.

The role of alliances in policy analysis is understudied, and a more typical approach would focus on other channels of impact, such as the rate of startup formation or the direct impacts on the flow of discovery research projects or candidates in development (as opposed to indirect impacts due to fewer alliances). These channels are likely to be less important in our context. R&D-based startups in the pharmaceutical industry are typically founded to commercialize academic findings, and given the difficulties associated with forecasting profitability at early stages of R&D, founding decisions likely depend more on the state of academic research than economic factors.

Zucker, Darby, and Brewer's (1998) results are consistent with this view: the availability of star scientists is positively associated with the number of startups formed each year, whereas the availability of venture capital and measures of the state of the economy are not. Given this, policy changes that impact profitability likely impact startup formation and the choice of projects to pursue less than in other contexts. Further, Danzon, Nicholson, and Pereira's (2005) results suggest that younger firms are less likely to abandon candidates in the face of bad economic prospects than older firms. Less experienced firms might not recognize weaknesses, or they might worry more about damaging the firm's image with potential investors than the ultimate impacts on profits. Highly specialized human capital might also make firms reluctant to abandon projects,

While startups might underemphasize prospects for profitability in their decision making, Nicholson, Danzon, and McCullough's (2005) results suggest that potential allies are uniquely positioned to assess these prospects. Potential allies have clear incentives to act on their information by forming alliances involving good projects and avoiding others, so policy changes that reduce profitability likely impact alliance formation. Policy changes might also impact contract terms (see Lerner and Merges 1998 and Higgins 2007 on the allocation of contractual rights in alliances), but we limit our scope to formation. For marginal alliances (where both parties are close to indifferent between pursuing the alliance and pursuing other opportunities) it will often not be possible to revise terms to satisfy both parties in the face of a decline in expected profits. Thus, we expect to see an impact of profit-reducing policies on alliance formation, and our empirical results suggest that such an impact occurs.

There was no generic pathway for "large" (primarily biological) molecules during the period we examine (1995-2007), so our tests allow for different impacts on traditional "small" molecules and large ones. However, as Paragraph IV challenges lead to more generics, the resulting lower prices reduce the prospective returns of all types of subsequent R&D in the affected classes, not just R&D involving small molecules, so we expect to see eventual impacts on large-molecule alliance formation. There are also factors other than the policy changes we consider that could cause the size-specific propensities for alliance formation to evolve in different ways over time. For example, the high prices received by some large molecules in rheumatoid arthritis and oncology during the period we examine likely made large-molecule alliances relatively more attractive in these areas. However, the critical issue for our analysis is whether large vs. small molecule opportunities in these or other areas shifted substantially in 1998 or 2000 (which seems unlikely). Beyond these considerations, firms likely anticipated that a generic pathway for large molecules would eventually emerge. Given that it takes an average of 12 years to go from initiating research to introducing a new approved drug (DiMasi, Hansen, and Grabowski 2003; DiMasi and Grabowski 2007), firms evaluating large-molecule projects late in our period might expect to face essentially the same IPR regime as small molecules by the time a marketable product would be available.

Our findings suggest there were impacts on small molecules initially and more widespread impacts later on. The 1998 event results in substantial long-term reductions in small-molecule alliance formation, while the 2000 event has a negative impact on all molecules. Limited evidence also suggests that the events increased alliance terminations, and terminations involving small molecules were affected more. The events reduced firm

value, and the impacts on young firms are comparable to those on large established firms. Portfolios in which firms lack previous alliances for their molecules in R&D suffer more, and for the 1998 event, firms with a greater fraction of small molecules in their R&D pipelines experience greater negative effects. On the whole, our results suggest that the reduction in expected patent protection reduced the incentives of strategic partners to form R&D alliances with young firms, and the value of the impacted firms fell. We conclude that a thorough assessment of the policy change inherent in the judicial decisions must consider impacts on R&D-based start-ups.

2. IPR Policy Changes and Paragraph IV Patent Challenges

The time a drug spends in human clinical trials has been rising for decades (DiMasi, Hansen, and Grabowski 2003). Firms typically apply for one or more patents involving their molecules prior to beginning Phase 1, so much of the patent life of a new molecule is used up during the development period. The resulting reduction in expected profits reduces the incentive to undertake R&D. The Drug Price Competition and Patent Term Restoration Act of 1984 (commonly referred to as the Hatch-Waxman Act) addressed this problem by extending the patent life of innovator drugs. Policy makers recognized the basic Nordhaus tradeoff described above, so they also included the abbreviated new drug application (ANDA) approval process, which allows generic drugs to be approved without going through clinical trials. Prior to the Hatch-Waxman Act, generic firms would typically have to wait until the innovator's patent expired to even begin clinical trials on their generic copies (assuming, as was typical, that rights would not be licensed by the patent-holder). After the amendment, generics were only required to satisfy the

lesser requirement of bioequivalency, and their efforts were permitted to begin well prior to patent expiration, so generic drugs could be marketed as soon as patents expired.

For our study, the Hatch-Waxman Act's requirements regarding IPR are of particular concern. Our summary draws from three main sources: www.paragraphfour.com (accessed December 2008), FDA (1998), and FTC (2002). Under the Hatch-Waxman Act, innovators are required to list their drug-specific patents in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book). When a generic firm files an ANDA, it makes one of four possible claims. The first is that there are no patents listed in the Orange Book. The second is that the listed patents have expired. The third is that the FDA should grant approval effective after the date the last patent expires. The fourth, which is the Paragraph IV filing, is that either the generic product does not infringe on the listed patents or that those patents are not enforceable. We focus on Paragraph IV filings.

If a generic firm is the first to file its ANDA with a Paragraph IV certification and is successful, it is granted a 180-day period of market exclusivity that begins either from the date of the first commercial marketing of the generic or from the court decision declaring the patents invalid or not infringed, whichever comes sooner (once the innovator is notified of the generic firm's Paragraph IV filing it has 45 days to file a patent infringement action against the generic firm). During the 180-day exclusivity period, no competing generic firms can produce the drug. Of course, even with the FDA’s grant of exclusivity, generic firms still face risks if they enter prior to success in the patent dispute, and penalties for infringement can result in payments to the patent-holder of up to three times actual damages. Because of this, generic firms typically wait

to market their drug until either a court has decided in their favor or it becomes clear the innovator will not file for infringement.

The 180-day exclusivity period provides a strong incentive to be first to file, because avoiding other generic competition results in exceptional profits. Grabowski and Vernon (1992, 1996) find that the average branded price immediately prior to patent expiration is six times the generic price after generics have diffused, and Grabowski and Kyle (2007) show that on average, 4-7 generic firms begin producing generic versions of the off-patent product in the year following patent expiration. Such dramatic price reductions and rapid entry quickly deplete above-normal profits. In contrast, under generic exclusivity, all the generic firm must do is slightly undercut the price of the branded competitor in order to obtain a large market share, and it can enjoy a high markup and high profits for a 6-month period. The generic firm's market share would also benefit from state-level drug substitution laws that encourage or require pharmacists to issue generics instead of brand-name drugs (Vivian 2008 provides a summary of the different state laws).

Prior to 1998, the FDA interpreted the Paragraph IV requirement to mean that a generic challenger must be sued by the patent holder and win before being granted 180-day exclusivity. The FDA's argument for this "successful defense" requirement was that it would eliminate the incentive for frivolous claims of patent invalidity or non-infringement, because otherwise an ANDA applicant might get exclusivity even if the applicant was unsuccessful in the lawsuit (FDA 1998). The successful defense requirement was challenged in *Mova Pharmaceutical Corp. v. Shalala*, 955 F. Supp. 128 (D.D.C. 1997) and *Granutec, Inc. v. Shalala*, No. 5:97-CV-485-BO(1) (E.D.N.C. July 3,

1997). FDA (1998) summarizes the outcomes: In *Granutec*, the U.S. Court of Appeals for the 4th Circuit held that the FDA's interpretation of the Hatch-Waxman Act's requirements was unsupported by the Act. The district court in *Mova* held that generic exclusivity should be granted to the first ANDA applicant who files a paragraph IV certification, regardless of whether the applicant is subsequently sued for patent infringement. The *Mova* decision was upheld in the U.S. Court of Appeals for the District of Columbia Circuit, and on June 1, 1998 (the first event date in our analysis), the district court in *Mova* entered an order permanently enjoining the FDA from enforcing its successful defense requirement. In response, the FDA removed the successful defense requirement and announced in FDA (1998) that it would make decisions on 180-day generic exclusivity on a case-by-case basis.

The Federal Trade Commission (2002) summarizes the impacts of the 1998 event up to 2002. Prior to 1992, the FDA granted 180-day exclusivity to only 3 generic applicants. In the period 1992-98, 180-day exclusivity was not granted at all. In contrast, in the period following the 1998 policy change until mid-2002, the FDA granted 180-day exclusivity to the first generic applicant for 31 drug products. The policy change has had lasting effects. Higgins and Graham (2009) describe trends in the number of Paragraph IV challenges in recent years. In the years 2001-2008, there were 35, 33, 96, 90, 81, 87, 162, and 165 Paragraph IV challenges involving 243 drugs.

The second event we consider is Barr Laboratories' successful challenge of Eli Lilly's Prozac/fluoxetine patent. This was the first time a blockbuster drug lost exclusivity as a result of a Paragraph IV challenge, and the high profits at stake increased generic firms' enthusiasm for this pathway. As Higgins and Graham (2009) discuss, such high

profile challenges are now standard procedure for generic firms. Barr filed its ANDA with a Paragraph IV certification in 1996, and on August 9, 2000 (the second event date in our analysis), the Court of Appeals vacated a lower court decision, ruled in favor of Barr, and invalidated one of the patents for Prozac. Eli Lilly's stock market value plummeted more than 29% and Barr's jumped 66% on the day of the decision. After the remaining patent expired, Barr launched its generic. Barr's 20mg-strength generic reached a 46% market share in the first month, 65% in two months, and by the end of Barr's exclusivity period, Prozac's market share had been eroded by 82% (paragraphfour.com, accessed December 2008). After other generics entered, fluoxetine fell from accounting for 31% of Barr's revenues to 1% of its revenues, so its successful Paragraph IV filing clearly helped it during the exclusivity period (paragraphfour.com, accessed December 2008). Barr's success was a landmark event for generic firms.

3. Data

We focus on U.S.-based R&D-based biopharmaceutical firms during the period 1995-2007. We begin by imposing two criteria:

1. The firm is listed in *Mergent Online* as being located in the US and belonging to Primary NAICS 3254 (Pharmaceutical and Medicine Manufacturing) (744 firms).

2. The firm has at least one drug in the *Pharmaprojects* database that meets the criteria discussed below (as discussed below, *Pharmaprojects* is a standard industry source that specializes in collecting and analyzing information on firm-level R&D pipelines in the

pharmaceutical industry). This step reduces the sample to 433 firms (several firms in NAICS 3254 are generic producers or other non-R&D-based manufacturers).

We consider a firm to be “young” or a “startup” (we use these terms interchangeably) if it was founded in the 10 years prior to the current year. Thus, for the year 1995, we use firms founded from 1985 to 1995. For 1996, we use 1986 to 1996, and so on, up to 2007, where we use firms founded from 1997 to 2007. Data on non-public firms is often missing in most databases, so for consistency we require every young firm to have an IPO in its first 10 years. Founding dates and IPO dates are collected from several standard sources, including *Compustat*, finance.google.com, *Hoovers*, *Lexis-Nexis*, *Mergent Online*, www.sec.gov, and finance.yahoo.com. This step yields 237 firms that are categorized as young in at least one year during our period. Other firms that are publicly traded at the point of observation are categorized as “established.”

For each young firm, we collect all drugs in the *Pharmaprojects* database that meet the following criteria:

1. The firm is listed as the "Originator" of the drug (to ensure the firm is the R&D firm and not just a licensee).

2. The drug is included in the "Trends" part of the database (the part that tracks progress of drugs through preclinical and clinical stages by year). We use this information to stop following drugs once they exit Phase 3 of development (to proceed toward launch) or cease development, and we also exclude drugs whose development has been suspended

the entire time they are tracked. Thus, the analysis focuses on drugs in R&D and alliances formed while drugs are in R&D.

3. A "Drug Profile" is available for the drug. The drug profile provides information on licensing, sales, and other alliance and acquisition activity. It also provides sufficient detail to fill in gaps in the "Trends" data.

4. The drug is identified as either a "large molecule" or a "small molecule" in the database. Virtually all drugs fall into one of these two categories (a small fraction are categorized as natural products or not applicable). *Pharmaprojects* considers "large molecules" to include all biological products along with "Chemical, synthetic, peptide" and "Chemical, synthetic, nucleic acid" products. "Small molecules" are all other chemical products.

We track each drug originated by a young firm from the time *Pharmaprojects* becomes aware of it (which is typically well before the drug enters human clinical trials) until either the drug leaves Phase 3, development is discontinued, or the firm ceases to meet our definition of young (or until the end of the sample period). *Pharmaprojects*'s business is selling information on R&D pipelines, so it aims to be comprehensive. Sources include contacts with firms, press releases, SEC filings, and conference presentations. However, it is likely that some early-stage drugs that firms keep to themselves are missed. Firms have little incentive to reveal the subject matter of their research efforts to outsiders and might prefer keeping such information from competitors.

If the absences are random as to molecule size and time period (which seems likely), this does not bias any of our results. Even if the sampling of drugs is somehow biased, our results on the propensity to form alliances should still be representative of the larger population unless *Pharmaprojects'* coverage systematically varies by the propensity for particular molecule sizes to involve alliances in particular time periods. Alliances are private transactions between firms, but in this industry they are important enough that they are typically announced in press releases and included in both pre- and post-IPO SEC filings. Given this, it is likely that the data on alliances is as comprehensive as possible given the incentives for firms to keep their early efforts secret.

There are 1,812 drugs in our sample. The number of drugs per firm varies: 116 firms have 5 or fewer drugs in R&D during the sample period, 65 have from 6-10, 29 have 11-15, 14 have 16-20, and 13 have more than 20. For each drug, we use *Pharmaprojects*' Drug Profiles to obtain information on transactions involving new licenses, outright sales, and acquisitions of the entire firm. We focus on transactions involving firms and ignore those involving nonprofits. To simplify the discussion, we refer to all relevant transactions as alliances. We checked our set of alliances against those recorded by *Deloitte Recap*, and in the few cases where the date an alliance is formed differs in *Pharmaprojects* and *Recap*; we use the *Recap* date (*Recap*'s business has traditionally focused on its alliance database).

The policy changes we consider pertain to the US market, so we use the *Pharmaprojects* Drug Profiles to eliminate alliances that focus solely on non-US markets. The result is 595 alliances. Several drugs generate no alliances that include the US market during our period, and others generate multiple alliances. A drug can have more

than one license for the US market, because a given drug can be used for different diseases and conditions, come in different packages, etc. Alliances can also be formed in different time periods for the same drug. There are 6,098 drug-year observations in which no alliances are formed, 525 with 1 alliance, 26 with 2, 3 with 3, and 1 each with 4 and 5. At the drug level, 1,326 drugs have no alliances recorded during the time they are observed, 412 have 1 alliance, 55 have 2, 11 have 3, 3 have 4, 2 have 5, and 3 have 6.

4. Results

4.1. Alliance Formation

Table 1 provides the number of molecules in R&D, the number of alliances formed, and the average number of alliances formed per molecule by year and molecule size. Clearly, small molecules generate more alliances on average than large molecules prior to the 1998 and 2000 events and less afterward. Figures 1-3 confirm that the patterns of alliance formation in Table 1 are present in the subsamples of preclinical projects and drugs in clinical trials. Table 2 provides the number of observations broken down by phase and molecule type and year to confirm that the pattern does not appear to be due to particular stages of R&D being over- or under-represented; all phases and molecule types are present in all years. The results in Table 2 also suggest that the changes in the propensity to form alliances are not accompanied by any sort of sustained reduction in the flow of small molecules in any of the stages of R&D. Thus, as we argued in the introduction, the primary impacts of the policy changes we consider may be through alliance formation.

To assess whether the policy changes we consider could be the drivers of the trends we observe in alliance formation, we estimate negative binomial count data models where the unit of observation is an R&D project involving a particular molecule

in a particular year and the dependent variable is the number of alliances formed in the year. The negative binomial model is the standard econometric model when the dependent variable is a count (0, 1, 2, etc.); it nests the simpler Poisson model but does not impose the restrictive assumption of the Poisson that the variance must equal the mean (see Cameron and Trivedi 2005). Formally, the conditional mean number of alliances formed involving a particular drug in a particular year is a function of the variables of interest and a drug-year-specific shock:

$$E(y_{it}) = \exp(\beta' x_{it} + \varepsilon_{it}) = \gamma_{it} u_{it}, \quad (1)$$

where y_{it} is the number of alliances formed, β is a parameter vector, x_{it} is a vector of independent variables, $\gamma_{it} = \exp(\beta' x_{it})$ and $u_{it} = \exp(\varepsilon_{it})$. Under the assumption that u_{it} has a gamma distribution with mean 1 and variance α, the density of y_{it} conditional on x_{it} has conditional mean γ_{it} and conditional variance $\gamma_{it}(1+\alpha\gamma_{it})$, where α measures over-dispersion relative to the Poisson distribution.

Our main independent variables are a small molecule dummy (that we include in all of our models to allow the initial propensities for alliance formation to vary by molecule size) and dummies for all possible annual break effects (after-1995, after-1996, and so on up to after-2006). We interact the small molecule dummy with the break effects to allow for the possibility that break effects differ for large and small molecules. We choose which breaks to include using a procedure similar to the one proposed by Quandt (1960) and summarized by Hansen (2001) for testing for structural breaks when the break dates are unknown. We first test for all possible break dates individually in turn. In each case, we include both the break effect and the break effect interacted with the small molecule dummy. Then we select the variable with the largest *t* statistic out of all the

variables tested, include it in the model, and repeat the procedure for all other possible break effects. We continue until no further breaks are statistically significant.

As Hansen (2001) discusses, if the break dates are truly unknown, standard critical values for test statistics are inappropriate, because the implicit mining of the data would have to be taken into account. We employ standard critical values, because in our case we have particular break points in mind (the 1998 and 2000 events), and we are using the procedure primarily as a reasonable way to assess whether our candidate break points would emerge from a neutral process. They do. In the first round, the after-1998 break effect interacted with the small molecule dummy comes into the model. In the second round, the after-2000 break effect comes into the model. In the third round, the after-1997 break effect interacted with the small molecule dummy comes in. Nothing further enters the model, and the after-1998 effect interacted with the small molecule dummy becomes insignificant, so we drop it. Thus, our results suggest a break in late 1997 or early 1998 that affects small molecules and an overall break in late 2000 or early 2001 that affects all molecules. These breaks are consistent with the events we focus on; our first event occurs in early 1998 and the second occurs in late 2000.

Table 3 provides the results. Column (1) presents the model that emerges from the Quandt-style selection process. Column (2) confirms that the breaks remain relevant when control variables are included. Repeating the Quandt-style process while including the control variables does not change our conclusions about breaks, although there is some evidence of a slight upturn in alliance formation in 2000 that is immediately overturned by the substantial negative break effect in 2001. As the possibility of a slight upturn does not impact our conclusions, we ignore it in what follows.

Our controls include several factors that might impact alliance formation. We include an indicator variable that measures whether any alliances have formed involving the drug prior to the current year. Approximately 49% of the drug/year observations have at least one previous alliance. Perhaps surprisingly, the coefficient on this variable is positive, which suggests that there is a bandwagon effect or an unmeasured quality effect that overwhelms any tendency for alliances to be substitutes for each other. To attempt to measure the quality of the drug, we include a dummy that indicates that *Pharmaprojects* forecasts the drug to have high sales potential. *Pharmaprojects* assigns drugs to one of five categories; the dummy indicates that the drug is in one of the highest two categories. Approximately 20% of the drugs in the sample have high sales potential. As expected, the results indicate that drugs with high sales potential are more attractive to potential allies. We also include dummies that indicate whether the drug is in phase 1, 2, or 3 in the year. We assign drug-year observations to phases using *Pharmaprojects*' system, which assigns a drug to a phase in a year if the drug enters that phase in the first quarter of the year. The non-included category is a drug that has not yet entered clinical trials, and this preclinical category accounts 4,591 of the observations in the sample. The results suggest that drugs in phase 3 tend to form more alliances, and this is not surprising. Funding is essential because phase 3 is the most expensive phase of human clinical trials, and given that phase 3 is the last phase prior to seeking approval for marketing, managing the regulatory process is critical. In addition, it is important to begin planning large-scale manufacturing and marketing. Allies can assist with all of these requirements.

Some firms, whether because of their location, contacts, or other firm-specific effects, are more or less likely to form alliances. Column (3) includes fixed firm effects to

allow for firm-specific factors that might affect alliance formation. The analysis excludes 62 firms that never formed any alliances during the sample period. The impacts of the 1998 and 2000 events become stronger. In unreported results, we also considered a model with drug-specific effects. Using fixed effects is inappropriate in this case, because any drug that never generates an alliance is effectively removed from the sample, and it is particularly important to include such drugs in our exercise. We estimated a random effects model. The test of the null of zero individual effects strongly failed to reject, and because of this the estimated coefficients were essentially the same as Column (2).

It is straightforward to use the estimates in Table 3 to compute how the average number of alliances formed each year varies by molecule type and period; we use the estimates from column (1) to illustrate the calculations. Initially, small molecules form an average of $Exp(-2.27+.39)=.15$ alliances per year, and large molecules tend to form less: $Exp(-2.27)=.10$. After 1997, roles are reversed because of the first break effect, and small molecules form an average of $Exp(-2.27+.39-.50)=.093$ alliances per year. After 2000, both types of projects form less alliances: $Exp(-2.27+.39-.50-.31)=.068$ for small and $Exp(-2.27-.31)=.076$ for large.

The 1998 and 2000 events might have also impacted decisions to terminate existing alliances, but measurement difficulties discourage us from providing more than a cursory analysis. Often termination coincides with abandoning R&D, and in such cases we cannot tell whether the termination decision preceded the abandonment decision or the other way around. Beyond this issue, as bad news, alliance terminations do not receive the same enthusiastic disclosure as alliance formation events, so the data on terminations is likely less complete. Incompleteness should not bias the sample toward

finding more terminations around the 1998 and 2000 events, so we briefly assess the 86 alliance termination events we observe that are distinct from project termination events. The results are consistent with terminations rising after the 1998 and 2000 events and with small molecules being affected more than large ones. In the years 1995-97, an average of 5.0 large molecule alliances and 2.7 small molecule alliances were terminated. In the years 1998-2002, the large-molecule average is slightly lower (4.6) and the small-molecule average is substantially higher (4.4). We include years 2001 and 2002 in this intermediate period to allow terminations to occur with a lag in response to the 1998 and 2000 events. Contractual restrictions could result in delay, or firms might wait until right before major expenditures to exercise the option to terminate. It makes sense that terminations would fall after vulnerable alliances get terminated, and in the years 2003-2007, both averages are lower, and terminations of small molecule alliances (1.8) exceed those for large molecules (1.2).

4.2 Impacts of the Events on Firm Value

We use event studies to assess the impacts of the June 1, 1998 and August 9, 2000 judicial decisions on firm value. The methodology of event studies is described by MacKinlay (1997). In our case, all firms experience the same events, so combining firms into portfolios is a reasonable way to proceed. We begin by constructing two portfolios. The first consists of the 48 young firms that are publicly traded on and before June 1, 1998. The second consists of the 49 young firms that are publicly traded on and before August 9, 2000. We exclude one outlier (on August 9, 2000 Targeted Genetics Corp. experienced firm-specific events that resulted in a one-day increase in its stock market value by more than 33%). Both portfolios weight the returns of the member firms

equally, so the daily returns in the portfolio are the mean of the daily returns of the firms, and our estimates capture the typical impact of the event on a young firm. With each portfolio, we estimate factor models using the 250 trading days (a calendar year's worth) that end 11 days prior to the event (it is common to leave several days prior to the event out of the estimation window to ensure that information leakage prior to the event does not contaminate the model of normal returns). The most general factor model is

$$R_{it} - R_{ft} = \alpha_i + \beta_i (R_{mt} - R_{ft}) + \gamma_{i1} SMB_t + \gamma_{i2} HML_t + \gamma_{i3} UMD_t + \varepsilon_{it} \quad (2)$$

where R_{it} is the daily return on portfolio i on day t, R_{ft} is the daily risk-free rate of return (estimated using the 1-month U.S. Treasury Bill), α_i, β_i, γ_{i1}, γ_{i2}, and γ_{i3} are parameters, R_{mt} is the daily return on the value-weighted market index provided by the Center for Research on Securities Prices (CRSP), SMB_t and HML_t are the Fama-French factors (Fama and French 1993, 1996), UMD_t is the momentum factor (Carhart 1997), and ε_{it} is the residual (the "abnormal return" in event study parlance). We obtained all of the data from Wharton Research Data Services (wrds-web.wharton.upenn.edu).

Using the estimated factor model coefficients and the data surrounding the event days, we compute the OLS residuals to estimate the abnormal returns for the days surrounding each event. We compute "cumulative abnormal returns" (CARs) by summing the OLS residuals across the days surrounding the event. A negative CAR indicates that the event resulted in lower-than-normal daily returns (the value of the portfolio falls below what is necessary to compensate investors for risk).

A potential problem with an event study like ours is that events other than the target event (the court decisions in our case) that occur on or around the same days

contribute to the CARs. We attempted to assess the potential importance of alternative events using Business Wire press releases from *Lexis-Nexis* (using the search term "pharmaceutical") but there are hundreds of press releases issued by industry firms each week (including financial announcements, management changes, alliances, etc.). While none appear to be good candidates for the results we obtain on their own (we found no other government policy changes or important court decisions), the aggregate impact of their combination is impossible to assess. Our implicit assumption is that the CARs we report can be attributed to the court decisions. A related concern is that, given that our analysis of alliance formation uses annual data, other events occurring during the year might contribute to the reduction in alliance formation we observe. While we are not aware of any specific alternative events, there are many days during our estimation windows with negative CARs, and we cannot be certain that we have isolated the only events that contributed to the reduction in alliance formation.

Table 4 provides the estimated coefficients of the factor models and the estimated CARs. We follow convention and refer to the event day as day 0 (June 1, 1998 for our first event and August 9, 2000 for our second event). CAR[0,0] is the value of the OLS residual on the event day. CAR[0,1] sums the OLS residuals on the event day and the day after. As MacKinlay (1997) discusses, [0,1] is the main window event studies consider, because it is possible that the full impact of announcements made late in the day are not realized until the following trading day. It is also common to consider some wider event windows, because information might leak out in advance of an event or take time to be fully understood and incorporated into stock prices, and we report CAR[-1,1] (the 3-day

window that runs from the day prior to the event to the day after) and CAR[-3,3] (three days prior to three days after).

Columns (1) and (3) of Table 4 report estimates based on the traditional market model described by MacKinlay (1997) that includes only the excess returns on the value-weighted index $(R_{mt} - R_{ft})$ as a factor. Columns (2) and (4) add the Fama-French factors and momentum. The additional factors are included to assess whether any event effects we observe using the market model might be explained by sources of risk left un-captured by the market model. The CARs are all negative and the impacts appear to be substantial, but statistical significance is elusive, and the 1998 results suggest that some of the negative impact obtained using the traditional market model might be due to factors left out of the model. Assessing significance is challenging because of the difficulties associated with computing the appropriate variance of the CARs under the null hypothesis that the event has no impact. We follow the traditional approach described by MacKinlay (1997) and compute the variance of the OLS residuals during the estimation window to estimate the variance of daily abnormal returns during the event window under the null. The variance of the CAR is computed by multiplying the estimated variance of daily abnormal returns by the number of days included in the CAR (under the null, the shocks are assumed to be independent across time, so covariances need not be considered). There are two potential problems with this approach in our context. First, there is entry into the portfolios during the estimation windows, and this could lead to heteroskedasticity. To address this concern, we confirmed that we obtain similar results to those in Table 4 if we estimate the factor models and CARs using only those firms that were publicly traded throughout the estimation window. Second,

Breusch-Godfrey tests indicate that the residuals of the market model for the 2000 event are autocorrelated. This appears to be due to missing factors, because the residuals of the full factor model show no evidence of autocorrelation. The estimated CARs are similar in both cases, and we focus on the full factor model in what follows.

Our next step is to compare the impacts of the events on young firms to those on established firms. The methodology in Table 5 is the same as Table 4 except that the sample includes all established (non-young) firms that were publicly traded on the event days except for six firms identified by Mergent Online as being primarily generics manufacturers (some large firms engage in new drug development as well as generic manufacturing). The portfolio is value-weighted to focus on large firms. For the 2000 event, we also exclude Barr Laboratories, the firm that prevailed against Eli Lilly, and we report results with and without Eli Lilly included in the portfolio. As we noted above, on August 9, 2000, Eli Lilly lost almost 1/3 of its value, so including it makes a substantial difference. The basic conclusion is that the magnitudes of the CARs are comparable to those in Table 4 as long as we ignore the impacts on the firm specifically targeted by the 2000 event. In both cases, large standard errors prevent us from asserting statistical significance, but the point estimates suggest the events have substantial impacts on value.

We turn to assessing the impacts of the events on each young firm individually. This allows us to assess whether the portfolio effects in Table 4 are widespread within the portfolios or due to a minority of firms experiencing substantial negative impacts. In these regressions we continue to impose that the parameters of the factor model are the same for every firm. This ensures that the parameters take on reasonable values and that our results are not driven by the imprecise estimates of these parameters that can result

from estimating factor models using data on individual firms (especially young ones, who often have highly volatile returns). Using the traditional market model, 35 of 48 CAR[0,1] effects in 1998 are negative and 33 of 49 effects in 2000 are negative. Under the null of no event impact, randomness ensures that only about half of the effects should be negative. If we regard the CARs as independent random draws under the null, then a simple test statistic can be used to assess significance (see MacKinlay 1997):

$$\theta = \left[\frac{N^-}{N} - .5 \right] \frac{\sqrt{N}}{.5} \tag{3}$$

where N^- is the number of negative effects and N is the total number of effects. Under the null of no effect, θ has a standard normal distribution. The two statistics in our case are 3.18 (significant at 1%) and 2.43 (significant at 5%). If we include the Fama-French and momentum factors as controls, we fail to reject the null that the 1998 event had no impact using the sign test, but we continue to reject the null that the 2000 event had no impact at the 1% level.

Our results on alliance formation suggest reasons why the events might not harm all firms equally and why we might get weak results from the sign test in 1998. First, if one of the key channels of impact is through alliance formation, then firms that already have alliances are cushioned from experiencing the full impact of the events. Second, the 1998 event should impact firms with more small molecules in their R&D pipelines more. To assess the first possibility, we examine each firm's drugs in R&D in the event years and compute the fraction that lack previous alliances. To assess the second, we compute the fraction involving small molecules. Then we construct portfolios that restrict the fraction that lack previous alliances and the fraction involving small molecules. Tables 6 and 7 report the sign tests and estimated CARs in each case. For brevity, we do not report

the factor model coefficients. The first set of entries repeat the CARs from Table 4 and the results of the sign test using the full factor model. The next column provides the results when only firms that lack some previous alliances (Table 6) or that have some small molecules in their R&D pipeline (Table 7) are included in the portfolio. The next column requires that more than 25% of the firm's drugs lack previous alliances (Table 6) or are small molecules (Table 7). The remaining columns use cutoffs of 50%, 75%, and 100%. The general pattern in Table 6 is that when the portfolio lacks more previous alliances, a higher fraction of firms experience negative effects, and the average impact of the events is more negative. Of the 40 cells that restrict the portfolio based on a lack of previous alliances, only 2 have a CAR that is less negative that the CAR in the unrestricted portfolio, and both of these occur when the portfolio is restricted the least. In Table 7, the general pattern for the 1998 event is that when the portfolio contains more small molecules, a higher fraction of firms experience negative effects, and the average impact of the events is more negative. None of the restricted CARs for the 1998 event are less negative than the unrestricted CARs. As expected given that the 2000 event appears to have impacted alliance formation for all molecule sizes, the results for the 2000 event do not suggest a greater impact on small molecules.

As a final step, we used event studies of alliance formation announcements to confirm that alliances create value in our sample. We use the 165 alliances for which we observe the exact day the alliance is announced (in other cases only an estimate is available, and event study methods require that we observe the exact day). Using the full factor model (imposing the same parameter vector for all firms as above) the CAR[0,1] is 2.7% (significant at the 1% level). We obtain similar results using the market model, and

the basic finding of substantial positive effects is robust to changing the event window. This suggests that at least some of the value reduction associated with the judicial decisions was due to investors anticipating a reduction in alliance formation.

5. Conclusion

This study considers an understudied policy maker (the judiciary) and an understudied mechanism of effect (alliance formation) in the arena of innovation policy. The evidence suggests that key 1998 and 2000 court decisions reduced the propensity of young R&D-based firms to form alliances. The 1998 event impacted small molecules, and the 2000 event impacted all molecules. The evidence also suggests that the court decisions reduced the value of young R&D-based firms. Firms that lacked previous alliances for their molecules in R&D suffered more, and for the 1998 event, firms with more small molecules in their R&D portfolio suffered more. Our results reveal an important consequence of the court rulings: small innovative firms are less viable, at least in part because it is more difficult to form alliances.

Future analyses of policy changes in settings with R&D-based startups should consider the welfare implications of impacts on alliance formation. Some work in this vein has already begun. Danzon, Nicholson, and Pereira (2005) find that alliances are associated with substantial increases in the probability of success in development. This suggests that policies that impact alliance formation ultimately impact the flow of new drugs and thus the health of consumers. Filson (2009) uses their empirical results to help parameterize a computable dynamic industry equilibrium model that highlights the impacts of policies on alliance formation and the resulting impacts on the flow of new drugs and finds substantial welfare effects associated with this channel.

References

Cameron, A. Colin, and Pravin K. Trivedi *Microeconometrics*: *Methods and Applications* (New York: Cambridge, 2005).

Carhart, Mark M. "On Persistence in Mutual Fund Performance" *Journal of Finance* 52:1 (March 1997): 57-82.

Danzon, Patricia M., Sean Nicholson and Nuno Sousa Pereira "Productivity in Pharmaceutical-Biotechnology R&D: The Role of Experience and Alliances" *Journal of Health Economics* 24:2 (2005): 317-39.

DiMasi, Joseph A., and Henry G. Grabowski "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics* 28 (2007): 469-79.

DiMasi, Joseph A., Ronald W. Hansen, and Henry G. Grabowski "The Price of Innovation: New Estimates of Drug Development Costs" *Journal of Health Economics* 22 (2003): 151-85.

Fama, Eugene F., and Kenneth R. French "Common Risk Factors in the Returns on Stocks and Bonds" *Journal of Financial Economics* 33 (February 1993): 3-56.

Fama, Eugene F., and Kenneth R. French "Multifactor Explanations of Asset Pricing Anomalies" *Journal of Finance* 51 (March 1996): 55-84.

Federal Trade Commission "Generic Drug Entry Prior to Patent Expiration: An FTC Study" July, 2002. Available at www.ftc.gov, accessed December 31, 2008.

Filson, Darren "The Impacts of Public Policies on Alliance Formation and the Evolution of Industry Performance: A Computable Dynamic Equilibrium Model with an Application to the Pharmaceutical Industry" Robert Day School of Economics and Finance, Claremont McKenna College working paper, 2009.

Food and Drug Administration, Center for Drug Evaluation and Research "Guidance for Industry: 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act" June, 1998. Available at www.fda.gov, accessed December 31, 2008.

Grabowski, Henry G. and Margaret Kyle "Generic Competition and Market Exclusivity Periods in Pharmaceuticals" *Managerial and Decision Economics* 28:4-5 (June-August 2007): 491-502.

Grabowski, Henry, and John Vernon “Brand Loyalty, Entry and Price Competition in Pharmaceuticals After the 1984 Drug Act” *Journal of Law and Economics* 35 (1992): 331-50.

Grabowski, Henry, and John Vernon “Longer Patents for Increased Generic Competition in the U.S.” *PharmacoEconomics* v10, Supp., n2 (1996): 110-23.

Hansen, Bruce E. “The New Econometrics of Structural Change: Dating Breaks in U.S. Labor Productivity” *Journal of Economic Perspectives* 15:4 (Autumn 2001): 117-28.

Higgins, Matthew J. “The Allocation of Control Rights in Pharmaceutical Alliances” *Journal of Corporate Finance* 13:1 (March 2007): 58-75.

Higgins, Matthew J. and Stuart J.H. Graham “Balancing Innovation and Access: Patent Challenges Tip the Scales” *Science* 326 (October 16, 2009): 370-71.

Lerner, Josh, and Robert P. Merges "The Control of Technology Alliances: An Empirical Analysis of the Biotechnology Industry" *Journal of Industrial Economics* 46:2 (June 1998): 125-56.

MacKinlay, A. Craig "Event Studies in Economics and Finance" *Journal of Economic Literature* 35 (March 1997): 13-39.

Murphy, Kevin M., and Robert H. Topel “The Economic Value of Medical Knowledge” in R.H. Topel and K.M. Murphy, eds., *Measuring the Gains from Medical Research: An Economic Approach* (Chicago: University of Chicago Press, 2003).

Murphy, Kevin M., and Robert H. Topel “The Value of Health and Longevity” *Journal of Political Economy* 114:5 (October 2006): 871-904.

Nicholson, Sean, Patricia M. Danzon and Jeffrey McCullough "Biotech-Pharmaceutical Alliances as a Signal of Asset and Firm Quality" *Journal of Business* 78:4 (2005): 1433-64.

Nordhaus, William D. *Invention, Growth, and Welfare: A Theoretical Treatment of Technological Change* Cambridge, MA: MIT Press, 1969.

"Paragraph Four Explained" Parry+Ashford Inc. 2006. Available at www.paragraphfour.com, accessed December 31, 2008.

Quandt, Richard “Tests of the Hypothesis that a Linear Regression Obeys Two Separate Regimes” *Journal of the American Statistical Association* 55 (1960): 324-30.

Solow, R. "Technical Change and the Aggregate Production Function" *Review of Economics & Statistics* 39 (1957): 312-20.

Vivian, Jesse C. “Generic-Substitution Laws” *U.S. Pharmacist* 33:6 (2008): 30-4.

Zucker, Lynne G., Michael R. Darby and Marilynn B. Brewer “Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises” *American Economic Review* 88:1 (March 1998): 290-306.

Table 1. Summary Statistics: Large vs. Small Molecules

Year	Number of large molecules in R&D	Number of alliances formed involving large molecules	Average number of alliances formed per drug for large molecules	Number of small molecules in R&D	Number of alliances formed involving small molecules	Average number of alliances formed per drug for small molecules
1995	236	32	0.14	188	27	0.14
1996	250	19	0.076	244	38	0.16
1997	246	25	0.1	291	45	0.15
1998	254	18	0.071	261	21	0.08
1999	257	27	0.11	262	22	0.084
2000	277	39	0.14	274	27	0.099
2001	292	17	0.058	279	15	0.054
2002	276	15	0.054	306	28	0.092
2003	184	13	0.071	318	26	0.082
2004	174	21	0.12	347	21	0.061
2005	179	12	0.067	368	20	0.054
2006	161	15	0.093	297	14	0.047
2007	165	12	0.073	268	26	0.097

Table 2. Number of Observations by Stage of R&D and Molecule Type

Year	Preclinical Large	Preclinical Small	Phase 1 Large	Phase 1 Small	Phase 2 Large	Phase 2 Small	Phase 3 Large	Phase 3 Small
1995	177	117	18	20	35	30	6	21
1996	190	162	19	21	31	40	10	21
1997	172	201	33	26	34	40	7	24
1998	178	177	37	20	35	43	4	21
1999	178	184	31	17	42	38	6	23
2000	197	192	27	20	46	44	7	18
2001	207	189	34	27	38	42	13	21
2002	190	213	33	29	38	45	15	19
2003	131	232	15	26	31	44	7	16
2004	114	257	24	30	27	45	9	15
2005	112	261	30	34	27	55	10	18
2006	99	196	23	37	29	44	10	20
2007	104	161	24	39	27	52	10	16

Table 3. The Negative Binomial Model of Alliance Formation. The unit of observation is a molecule in a particular year. The dependent variable is the number of alliances formed in the year. The table entry is the coefficient, and the cluster-robust standard error (where each drug is a cluster) is in parentheses.

Variable	(1)	(2)	(3)
Constant	-2.27*** (.076)	-2.60*** (.096)	-3.10*** (.95)
The drug is a small molecule	.39*** (.13)	.31** (.13)	.40** (.17)
The drug is small molecule and the year is after 1997	-.50*** (.14)	-.44*** (.14)	-.71*** (.16)
The year is after 2000	-.31*** (.095)	-.30*** (.094)	-.71*** (.13)
The drug has at least one previous alliance		.45*** (.092)	.14 (.090)
The drug has high sales potential		.17* (.097)	.070 (.11)
The drug is in Phase 1		.12 (.13)	.14 (.15)
The drug is in Phase 2		.094 (.12)	.20 (.13)
The drug is in Phase 3		.46*** (.14)	.51*** (.17)
Fixed firm effects are included	No	No	Yes
The over-dispersion parameter of the negative binomial model	.58*** (.30)	.49** (.29)	0
The sample size	6,654	6,654	6,100
The log likelihood	-2,035	-2,016	-1,822

***, **, and * indicate significant at 1, 5, and 10% respectively

The significance levels on the over-dispersion parameters correspond to the p-values of the likelihood ratio tests that the over-dispersion parameter is zero. In the model with fixed firm effects, the estimated over-dispersion parameter is essentially 0, so the results are essentially those of a Poisson model.

Table 4. Event Studies of the Impacts of the June 1, 1998 and August 9, 2000 Events on Young Firms. The unit of observation is the equal-weighted portfolio of young firms on a particular day. The dependent variable is the return on the portfolio. The independent variables are risk factors that have been shown to help explain variation in stock returns. The factor model estimated using the 250 trading days that end 11 days prior to the event provides a model of normal returns, and the residuals are the abnormal return. The goal is to estimate the OLS residuals during the event window and sum them to estimate cumulative abnormal returns. CAR[0,0] is the OLS residual on the event day. CAR[0,1] includes the event day and the day after, CAR[-1,1] includes the day before as well, and CAR[-3,3] includes the 7 trading days surrounding the event. The statistical significance of the CARs is assessed using the estimated variance of the OLS residuals during the 250-day estimation window. Standard errors are in parentheses.

Variable	1998		2000	
	(1)	(2)	(3)	(4)
Factor model coefficients:				
Constant	.00021 (.00082)	-.000092 (.00079)	.0062*** (.0018)	.0053*** (.0013)
Market Excess Return	.62*** (.085)	1.05*** (.16)	1.24*** (.13)	1.84*** (.19)
SMB (the small-minus-big Fama-French factor)		1.07*** (.19)		2.53*** (.22)
HML (the high-minus-low Fama-French factor)		.12 (.27)		1.20*** (.29)
UMD (the Carhart momentum factor)		-.34 (.27)		-.036 (.21)
The number of observations	250	250	250	250
R-squared	.18	.29	.27	.66
Cumulative abnormal returns (CARs):				
CAR[0,0]	-.021* (.013)	-.0078 (.012)	-.0080 (.029)	-.015 (.020)
CAR[0,1]	-.032* (.018)	-.011 (.017)	-.017 (.050)	-.020 (.028)
CAR[-1,1]	-.025 (.022)	-.0074 (.021)	-.033 (.050)	-.036 (.034)
CAR[-3,3]	-.053 (.034)	-.030 (.032)	-.098 (.076)	-.097* (.052)

***, **, and * indicate significant at 1, 5, and 10% respectively

Table 5. Event Studies of the Impacts of the June 1, 1998 and August 9, 2000 Events on Large Established Firms. The unit of observation is the value-weighted portfolio of established firms on a particular day. The dependent variable is the return on the portfolio. The independent variables are risk factors that have been shown to help explain variation in stock returns. The factor model estimated using the 250 trading days that end 11 days prior to the event provides a model of normal returns, and the residuals are the abnormal return. The goal is to estimate the OLS residuals during the event window and sum them to estimate cumulative abnormal returns. CAR[0,0] is the OLS residual on the event day. CAR[0,1] includes the event day and the day after, CAR[-1,1] includes the day before as well, and CAR[-3,3] includes the 7 trading days surrounding the event. The statistical significance of the CARs is assessed using the estimated variance of the OLS residuals during the 250-day estimation window. Standard errors are in parentheses.

Variable	1998		2000		2000 Without Lilly	
	(1)	(2)	(3)	(4)	(5)	(6)
Factor model coefficients:						
Constant	.000094 (.00054)	.00067 (.00050)	.00033 (.0011)	.0012 (.00098)	.00021 (.0011)	.0011 (.00097)
Market Excess Return	1.24*** (.055)	.61*** (.10)	.60*** (.078)	.85*** (.15)	.63*** (.077)	.87*** (.15)
SMB (the small-minus-big Fama-French factor)		-.65*** (.12)		-.29* (.17)		-.27 (.17)
HML (the high-minus-low Fama-French factor)		-.75*** (.17)		-.21 (.22)		-.25 (.22)
UMD (the Carhart momentum factor)		.70*** (.17)		-.62*** (.16)		-.64*** (.16)
The number of observations	250	250	250	250	250	250
R-squared	.67	.74	.20	.37	.21	.38
Cumulative abnormal returns (CARs):						
CAR[0,0]	.00042 (.0084)	-.0033 (.0075)	-.052*** (.017)	-.049*** (.015)	-.022 (.017)	-.020 (.015)
CAR[0,1]	-.0050 (.012)	-.015 (.011)	-.044* (.024)	-.046** (.021)	-.013 (.024)	-.015 (.021)
CAR[-1,1]	-.016 (.014)	-.024* (.013)	-.046 (.030)	-.052** (.026)	-.018 (.029)	-.023 (.026)
CAR[-3,3]	.0025 (.022)	-.019 (.020)	-.079* (.045)	-.095** (.040)	-.052 (.045)	-.067* (.040)

***, **, and * indicate significant at 1, 5, and 10% respectively

Table 6. The Impact of the Lack of Previous Alliances on the Estimated Event Effects for Young Firms. The first column reports the outcomes of the sign test and the cumulative abnormal returns (CARs) that result from estimating the full factor model with all active firms. Subsequent columns re-estimate the results using portfolios that restrict attention to firms for which at least one drug in R&D has no previous alliances (noA > 0%), at least 25% of drugs in R&D have no previous alliances (noA > 25%), at least 50%, and so on. Standard errors are in parentheses.

	All Active Firms	noA > 0%	noA > 25%	noA > 50%	noA > 75%	noA =100%
The 1998 event:						
The number of firms	48	36	31	17	7	5
The fraction of firms with negative CAR[0,1]	50%	53%	58%	71%*	71%	80%
Portfolio CARs:						
CAR [0,0]	-.0078 (.012)	-.0069 (.014)	-.0085 (.016)	-.014 (.022)	-.021 (.021)	-.038 (.024)
CAR [0,1]	-.011 (.017)	-.017 (.020)	-.021 (.023)	-.032 (.031)	-.024 (.030)	-.043 (.034)
CAR [-1,1]	-.0074 (.021)	-.014 (.025)	-.020 (.028)	-.019 (.038)	-.025 (.036)	-.038 (.041)
CAR [-3,3]	-.030 (.032)	-.032 (.038)	-.039 (.042)	-.031 (.057)	-.072 (.056)	-.097 (.063)
The 2000 event:						
The number of firms	49	43	41	25	11	7
The fraction of firms with negative CAR[0,1]	67%**	70%***	73%***	76%***	73%	71%
Portfolio CARs:						
CAR [0,0]	-.015 (.020)	-.019 (.021)	-.020 (.021)	-.026 (.022)	-.021 (.027)	-.032 (.033)
CAR [0,1]	-.020 (.028)	-.028 (.029)	-.030 (.029)	-.038 (.031)	-.029 (.038)	-.038 (.047)
CAR [-1,1]	-.036 (.034)	-.043 (.036)	-.047 (.036)	-.064* (.038)	-.060 (.047)	-.059 (.057)
CAR [-3,3]	-.097* (.052)	-.096* (.055)	-.099* (.055)	-.12** (.058)	-.16** (.071)	-.16* (.087)

***, **, and * indicate significant at 1, 5, and 10% respectively

Table 7. The Impact of the Presence of Small Molecules on the Estimated Event Effects for Young Firms. The first column reports the outcomes of the sign test and the cumulative abnormal returns (CARs) that result from estimating the full factor model with all active firms. Subsequent columns re-estimate the results using portfolios that restrict attention to firms for which at least one small molecule is in R&D (SM > 0%), at least 25% of drugs in R&D are small molecules (SM > 25%), at least 50%, and so on. Standard errors are in parentheses.

	All Active Firms	SM > 0%	SM > 25%	SM > 50%	SM > 75%	SM =100%
1998 event:						
The number of firms	48	34	30	26	22	20
The fraction of firms with negative CAR[0,1]	50%	50%	53%	62%	64%	65%
Portfolio CARs:						
CAR [0,0]	-.0078 (.012)	-.012 (.013)	-.016 (.010)	-.019* (.011)	-.021* (.011)	-.024** (.012)
CAR [0,1]	-.011 (.017)	-.011 (.018)	-.014 (.014)	-.020 (.015)	-.018 (.016)	-.020 (.017)
CAR [-1,1]	-.0074 (.021)	-.014 (.023)	-.016 (.018)	-.022 (.018)	-.015 (.020)	-.022 (.021)
CAR [-3,3]	-.030 (.032)	-.036 (.035)	-.039 (.027)	-.046 (.028)	-.040 (.030)	-.052 (.032)
2000 event:						
The number of firms	49	43	37	29	25	21
The fraction of firms with negative CAR[0,1]	67%**	65%**	68%**	59%	52%	52%
Portfolio CARs:						
CAR [0,0]	-.015 (.020)	-.013 (.021)	-.015 (.021)	-.0070 (.021)	-.0023 (.022)	-.0040 (.024)
CAR [0,1]	-.020 (.028)	-.021 (.029)	-.025 (.030)	-.015 (.030)	-.0055 (.031)	-.0038 (.034)
CAR [-1,1]	-.036 (.034)	-.037 (.036)	-.040 (.037)	-.040 (.036)	-.031 (.038)	-.035 (.042)
CAR [-3,3]	-.097* (.052)	-.10* (.055)	-.098* (.056)	-.11** (.056)	-.10* (.058)	-.10 (.064)

***, **, and * indicate significant at 1, 5, and 10% respectively

Figure 1. Average Number of Alliances Formed per Drug, by Year

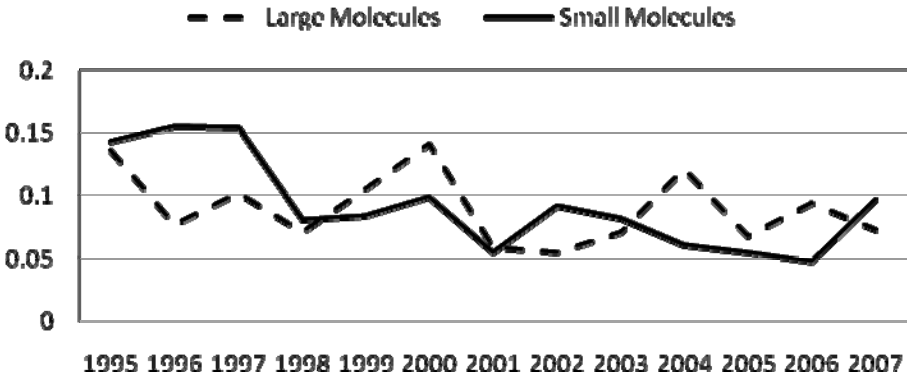

Figure 2. Average Number of Alliances Formed per Drug, by Year: Preclinical Drugs

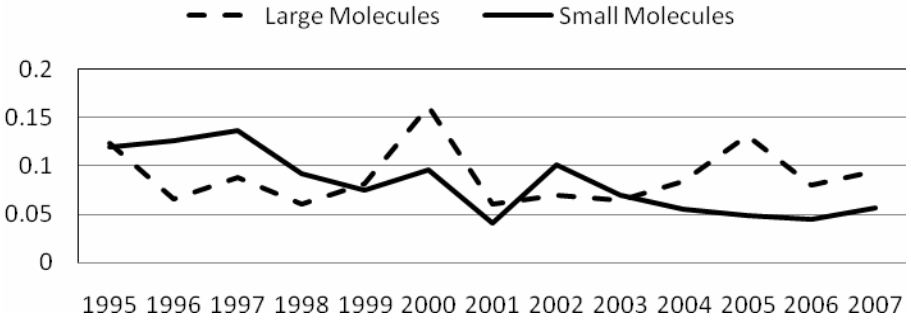

Figure 3. Average Number of Alliances Formed per Drug, by Year: Drugs in Clinical Trials