

THE OXFORD HANDBOOK OF

---

THE ECONOMICS  
OF THE  
BIOPHARMACEUTICAL  
INDUSTRY

*Edited by*

PATRICIA M. DANZON  
AND  
SEAN NICHOLSON

OXFORD  
UNIVERSITY PRESS

## CHAPTER 18

---

# MERGERS, ACQUISITIONS, AND ALLIANCES

---

HENRY G. GRABOWSKI AND  
MARGARET KYLE

THE pharmaceutical industry has been characterized by successive waves of merger activities and industry consolidation since the 1980s. There also has been a substantial out-sourcing of research and development (R&D) stage activities (i.e., vertical disintegration). An evolving market for innovation has emerged through numerous licensing and partnership agreements. These developments are connected to an intensified search for new therapeutic entities to replace older products that are subject to patent expiration and generic competition.

It is useful from a historical perspective to chronicle some of the key dynamic forces affecting the pharmaceutical industry. The passage of the 1984 Waxman-Hatch Act in the United States was an important legislative change that allowed generics to enter the market by demonstrating bioequivalence (i.e., without the need to do clinical tests of safety and efficacy) (Grabowski 2007). Competitive pressures intensified in the 1990s with the rise of buyer-side market power in the form of managed care organizations and pharmacy benefit managers (PBMs) in the United States and increasingly stringent price controls in other major world markets. The pharmaceutical industry also has been dealing with a declining trend in new molecular entities and R&D productivity since the mid 1990s (DiMasi et al. 2003; Cockburn 2006). The rapid loss of revenues to generics after patent expirations, combined with fewer new products being approved each year, has created a replacement problem for many large pharmaceutical firms.

One structural response to these dynamic forces has involved a series of large-scale mergers and acquisitions (M&As) as well as many smaller-scale acquisitions by pharmaceutical firms. The first merger wave began in the 1989–1990 period. The annual value of pharmaceutical mergers in those two years exceeded that of any prior year in the decade of 1980s (Ravenscraft and Long 2000). This was followed by an even larger merger wave that began in the mid-1990s and continued into the 2000s (Koenig and Mezick 2004; Danzon et al. 2007). After a relative lull for some years, two major mergers were consummated in 2009 (Pfizer-Wyeth and Merck-ScheringPlough).

Table 18.1 shows how the global market shares for biopharmaceutical firms changed between 1989 and 2009. Combinations included not only mergers between large pharmaceutical firms but also acquisitions of biotech firms by pharma firms and mergers between firms of different sizes in the emerging biotech sector. All the underlined companies consummated a major merger in the preceding 5- or 10-year period. Correspondingly, the starred companies were combined into larger entities between that period and the subsequent period of company rankings. Over the full span between 1989 and 2009, most of the top-ranked companies engaged in merger activity with other biopharmaceutical firms. There were also many smaller-scale M&As over this 20-year period.

Table 18.2 shows the M&As underlying Pfizer's family roots. Pfizer has completed three of the largest industry M&As over the past decades. As shown, Pfizer's three merger partners (Warner Lambert, Pharmacia, and Wyeth) had themselves undergone significant M&As prior to their integration by Pfizer. Other firms with a history of several M&As include GlaxoSmithKline (involving Glaxo, Burroughs-Wellcome, Smith Kline, and Beecham), and Sanofi-Aventis (involving Hoechst, Marion Merrell Dow, Aventis, Rhone-Polenc, and Sanofi-Synthelabs).

There has been a trend toward increased concentration in pharmaceuticals from M&As and other factors. Global shares for the top 10 firms increased to 45 percent by 2009, compared with 28 percent in 1989 (see Table 18.1). Concentration in the United States of the pharmaceutical preparation manufacturing industry is moderately higher than what global shares indicate, with an eight-firm concentration ratio of 53 percent in 2002 (the latest year available from the US Census Bureau), compared with 36 percent in 1987. Despite the increased merger activity, however, the pharmaceutical industry is still relatively unconcentrated compared to many other industry sectors.

Many changes in company rankings shown in Table 18.1 also resulted from new product introductions and patent expirations. This is reflected by the rapid growth of dedicated biotech firms such as Amgen<sup>1</sup> and of primarily generic firms such as

1. The sales of a second major biotech firm, Genentech, are included in Roche's sales in 1999 and 2004, because Roche acquired a majority equity interest in Genentech in 1990. Under the agreement, Genentech has operated as a freestanding company in the United States, with options on foreign licensing rights going to Roche on several of Genentech's products. Before Roche's acquisition of all the shares in 2009, the two

Table 18.1 Global shares and mergers in pharmaceuticals, 1989–2009.

Rank	2009		2004		1999		1989	
	Company	Share (%)	Company	Share (%)	Company	Share (%)	Company	Share %
1	<u>Pfizer</u>	<u>7.6</u>	<u>Pfizer</u>	<u>9.8</u>	Merck	4.5	Merck	4.0
2	<u>Merck</u>	<u>5.2</u>	<u>GlaxoSmithKline</u>	<u>6.3</u>	<u>AstraZeneca</u>	<u>4.4</u>	<u>BMS</u>	<u>3.5</u>
3	Novartis	5.1	<u>Sanofi-Aventis</u>	<u>5.2</u>	<u>Glaxo Wellcome*</u>	<u>4.1</u>	<u>Glaxo*</u>	3.1
4	<u>Sanofi-Aventis</u>	<u>4.7</u>	<u>J&amp;J</u>	<u>4.7</u>	<u>Pfizer*</u>	<u>4.1</u>	<u>SKB</u>	<u>3.0</u>
5	<u>GlaxoSmith Kline</u>	<u>4.7</u>	Merck	4.6	BMS	4.0	<u>Ciba-Geigy*</u>	2.9
6	<u>AstraZeneca</u>	<u>4.6</u>	Novartis	4.4	<u>Novartis</u>	<u>4.0</u>	<u>AHP*</u>	<u>2.7</u>
7	Roche	4.4	<u>AstraZeneca</u>	<u>4.2</u>	<u>Aventis</u>	<u>3.9</u>	<u>Hoechst*</u>	2.4
8	<u>J&amp;J</u>	<u>3.6</u>	Roche	3.4	<u>J&amp;J</u>	<u>3.8</u>	<u>J&amp;J</u>	2.3
9	Lilly	2.7	BMS	3.0	<u>AHP</u>	<u>3.1</u>	Bayer	2.3
10	Abbott	2.6	<u>Wyeth*</u>	<u>2.7</u>	<u>Roche</u>	<u>3.0</u>	<u>Sandoz*</u>	2.1
11	Teva	2.1	Abbott	2.7	Lilly	2.9	Lilly	2.1
12	Bayer	2.1	Lilly	2.4	<u>SKB*</u>	2.8	Pfizer	2.0
13	<u>Boehringer Ing</u>	<u>2.0</u>	Amgen	2.1	<u>Warner Lambert*</u>	2.8	<u>Roche*</u>	1.9
14	Amgen	2.0	Takeda	1.7	Abbott	2.6	<u>Schering-Plough</u>	1.6
15	Takeda	1.9	<u>Boehringer Ingel</u>	<u>1.6</u>	<u>Schering-Plough</u>	2.5	<u>MMD*</u>	1.6

16	BMS	1.9	Schering-Plough*	1.3	Bayer	2.0	Upjohn	1.5
17	Daiichi Sankyo	1.2	Bayer	1.2	Pharmacia Upjohn*	1.8	Boehringer Ingel	1.5
18	Novo Nordisk	1.1	Schering AG	0.9	Takeda	1.5	Warner Lambert	1.4
19			Eisai	0.9	Boehringer Ingel	1.4	Cyanamid*	1.4
20			Teva	0.8	Sanofi Synthelabo*	1.3	Abbott	1.4
21					Monsanto (Searle)	1.2	Zeneca (ICI)*	1.4
22					Sankyo	1.0	Wellcome*	1.2
23					Amgen	1.0	Shiongi	1.2
24					Schering AG	1.0	Takeda	1.2
25					Otsuka	0.8	Rhône-Poulenc Rorer	1.2

Notes: Underlined companies consummated a major merger in the preceding 5- or 10-year period. Companies marked with an asterisk (\*) were combined into larger entities during the preceding period.

Source: Authors' analysis based on IMS Health Care Market Share Data.

Table 18.2 Pfizer's family roots

Target or Merger Partner	Acquired By or Merged With	Completion Date	Final Value (\$USB)	Name of New Company
American Cyanamid	American Home Products	11/21/94	\$9.6	American Home Products (Wyeth on 3/11/02)
Upjohn	Pharmacia	11/2/94	\$7.0	Pharmacia & Upjohn
Warner-Lambert	Pfizer	6/19/00	\$114.7	Pfizer
Monsanto	Pharmacia & Upjohn	3/31/00	\$26.0	Pharmacia
Pharmacia	Pfizer	4/16/03	\$56	Pfizer
Wyeth	Pfizer	10/15/09	\$68	Pfizer

Source: Authors' analysis; completed dates and market values were obtained from Van Brunt (2009).

Teva.<sup>2</sup> These firms became part of the top 20 biopharmaceutical firms listed in Table 18.1 beginning in 2004. Conversely, some compression in the global shares of the top-ranked firms is apparent in the most recent period as patent expirations and generic competition have eroded the sales of the very largest firms. These factors in turn provide one of the primary motives for M&As, as discussed later.

Although M&As have tended to occur in waves, there has been continuous growth in the number and value of R&D stage alliances in the pharmaceutical and biotechnology industries. Alliances can be a substitute for M&As, but they also can be a forerunner to a future merger or acquisition between partners by serving to provide an extended period of due diligence. During the first decade of the 2000s, the number of alliances with market valuations of \$100 million or more increased several-fold between the beginning and ending years of the decade (Recombinant Capital 2008). This rapid growth in value reflects the fact that many deals are now broader in scope than a single compound or a related family of compounds. It also reflects increasing potential values for licensors associated with the intense competition for deals in hot therapeutic areas such as oncology (Ernst and Young Online 2011).

In this chapter, we consider the determinants and effects of M&As with a particular focus on innovation and R&D productivity. As noted, alliances can be either

companies had signed a joint-development, co-licensing option agreement for new drug candidates.

2. The generic drug industry has also experienced significant consolidation in recent years, with major acquisitions by Teva and other firms. The United States has the largest and fastest-growing generic market. In 2009, generic drugs accounted for three-quarters of all dispensed prescriptions in the United States (Berndt and Aiken, 2010).

a substitute or a longer-term complement to M&As. We also consider the empirical literature on the role of alliances and their effects on innovative performance. The final two sections consider policy-related issues and interesting questions for future research.

## DETERMINANTS OF MERGERS AND ACQUISITIONS

---

The motives for M&As in pharmaceuticals that have received attention in the economic literature can be put into five general categories: (1) response to industry-wide or company-specific shocks, (2) economies of scale and scope, (3) access to new technology, (4) expansion to foreign markets and other stages of the drug distribution chain, and (5) increased market power and size. In this section, we consider the evidence regarding motives for M&As in the pharmaceutical industry. It is important to understand the reasons for M&As before attempting to evaluate studies that are focused on their effects.

### Strategic Response to Industry-Wide or Company-Specific Shocks

The hypothesis that industry-wide shocks can precipitate merger waves appears to be a useful concept in understanding pharmaceutical mergers. The original hypothesis goes back to Michael Gort (1969). Industry-wide shocks appear to explain merger waves that have occurred in other industries, such as banking and telecommunications in the 1990s (Andrade et al. 2001). In the case of pharmaceuticals, the economic environment became more difficult by the late 1980s with increased price competition and declining R&D productivity.

A key prediction of the industry shocks hypothesis is that firms under economic stress are more likely to engage in mergers. An oft-cited firm-specific motivation for pharmaceutical M&As is to fill in gaps in a company's pipeline to maintain firm scale and growth in the face of patent expiration of a major product. Pharmaceutical products exhibit a highly skewed distribution of revenues and returns (Grabowski et al. 2002). Firms are dependent on a relatively small number of blockbuster products for a substantial portion of revenues. Patent expirations on major projects can produce rapid losses in unit sales to generic entrants and can leave firms with lower expected profits and substantial excess capacity in their production facilities and sales forces.

When profits and stock prices come under pressure from industry shocks, many affected firms are motivated to use their accumulated cash flows to acquire another firm's products and pipeline. The bidder often can recoup most or all of the premium associated with acquisitions by consolidating operations and cutting out the excessive infrastructure capacity associated with the two previously independent organizations. Various researchers also have made the point that M&As facilitate disruptive organizational change that would otherwise meet with substantial internal inertia and resistance (Ravenscraft and Long 2000). However, M&As are also associated with substantial integration costs that can affect the productivity of the firm in the post-merger period (Larsson and Finkelstein 1999; Clark 2001).

Ravenscraft and Long (2000) performed one of the first analyses of pharmaceutical mergers. Their study covered mergers of significant value undertaken between 1985 and 1996. Using event study methodology, they found that the large horizontal mergers and cross-border mergers created moderate gains in overall stock market value. As in other industry studies, however, target firms captured most of the returns. Their case study of the Glaxo-Wellcome merger also pointed to substantial disruption and transition costs in integrating the two firms.

Ravenscraft and Long's (2000) findings are consistent with the hypothesis that mergers are a response to industry shocks and excessive capacity. Their analysis of cost-cutting for large horizontal pharmaceutical mergers found a reduction in total headcount in the post-merger period ranging from 8 percent to 20 percent of the combined workforce in the pre-merger period. Although cost-cutting in manufacturing and marketing personnel were proportionately greater than for R&D employees, there also was a consolidation of R&D laboratories and the elimination of marginal R&D projects by several firms.<sup>3</sup>

The Ravenscraft and Long (2000) analysis, however, did not examine longer-term effects on the firms' R&D productivity or the probability of developing successful products. To the extent that these reductions in R&D activities eliminated duplicate efforts or projects with low probability of success, or facilitated more external alliances, the companies' R&D performance could have increased in the post-merger period compared to the pre-merger one. This issue is considered further in a later section.

Two recent analyses have found that patent expiration and the related pipeline gaps are important drivers of merger activity. A study of 202 biotechnology and pharmaceutical mergers between 1998 and 2001 found that pharmaceutical firms with a relatively old portfolio of marketed drugs exhibited a higher propensity to acquire another firm (Danzon et al. 2007). A second study of 160 pharmaceutical mergers between 1994 and 2001 found that firms with lower scores in the strength of their R&D pipeline and fewer years of exclusivity on their marketed drugs had a greater probability of engaging in a merger (Higgins and Rodriguez 2006).

3. An analysis by Centerwatch (2000) of 11 large mergers (22 pharmaceutical companies) that occurred between 1989 and 1998 also reported a 34 percent average reduction in development projects three years after the merger was consummated.

The fact that firms in economic stress are more likely to engage in mergers raises methodological issues in evaluating pharmaceutical merger activity. In particular, one cannot simply compare merging entities to overall industry performance or to the performance of firms that did not merge, because the decision to merge is almost certainly correlated with performance or other important (and often unobserved) factors. Rather, it is important to construct control groups with similar firm characteristics in evaluating the effects of a merger, to use instrumental variables to deal with the endogeneity of mergers and firm performance, or to estimate a structural model. We return to this point in a later section.

## Economies of Scale and Scope

In contrast to defensive company responses to industry shocks, there are several proactive motives for M&As. These include increases in size to achieve critical mass and economies of scale in R&D and other firm activities. Economies of scale are one of the most studied topics in the field of industrial organization, and they have been the subject of particular attention in the case of pharmaceutical R&D.

A pair of papers (Henderson and Cockburn 1996; Cockburn and Henderson 2001) focused on economies of scale and scope in drug R&D and provided some insight as to the effects of increased size on R&D productivity. These authors looked for the effect of scale and scope on productivity, at a research program level, for 10 large firms. The advantage to these papers is that the authors used extremely detailed data (including program-level R&D spending) over a very long time period. They concluded that firms engaged in a broader scope of research activities are more productive than focused firms, but that scale does not matter much once the scope is controlled for. However, it should be noted that their sample included only 10 firms, so generalization of their results, particularly to smaller firms, may not be appropriate. In addition, the measure of productivity used was a count of patents assigned to the firm. The granting of a patent occurs fairly early in the research process, and there may be substantial heterogeneity in the success of firms in converting patents into marketed products. A more recent paper by Danzon et al. (2005) found benefits from a company's development experience as measured by the number of drugs in clinical trials, but these benefits are also subject to diminishing returns. This study is discussed further in the section summarizing the effects of alliances on R&D productivity.

The consolidation of the larger pharmaceutical firms shown in Table 18.1 has been accompanied by increasing breadth in the R&D activities of the leading firms in the industry across therapeutic categories. For example, Pfizer, as a result of its large-scale mergers with Warner Lambert and Pharmacia, inherited R&D programs in new fields such as oncology, endocrinology, and ophthalmology. This complemented the company's historical strengths in anti-infectives and drugs for cardiovascular disorders, depression, and erectile dysfunction (Burns et al. 2005).

This increased breadth may lead to some benefits from economies of scope over time, as described in the academic literature by Cockburn and Henderson.

At the same time, Pfizer and other leading pharmaceutical firms now have multibillion-dollar annual R&D budgets and several hundred R&D projects to manage. At this scale, companies may have entered a region of diminishing returns, as size or scope benefits are offset by the challenges of managing and motivating creative individuals in a large bureaucracy. It is notable that Pfizer, in the aftermath of its large-scale merger with Wyeth, has focused its R&D in five major therapeutic areas and consolidated its R&D laboratories geographically around those areas. GlaxoSmithKline and other firms with similarly large R&D programs and D projects also are instituting more flexible organizational structures and delegating more decision-making authority to the heads of the various therapeutic areas (Dorey 2001; Mathieu 2007).

### Access to New Technologies

Beyond economies of scale, biopharmaceutical firms may engage in mergers to gain a presence in an emerging therapeutic category that represents significant future growth opportunities. For example, the oncology class has been characterized by a disproportionate number of "first-in-class" drug introductions (DiMasi and Grabowski 2007). The novel entities in this class have emerged primarily from the biotech sector, based on molecular biology techniques (e.g., new monoclonal antibody products and other targeted agents). Because it can take several years or even decades to build the internal scientific capability to enter a new therapeutic area or implement a new research platform in an emerging scientific field, mergers provide a more expeditious way to enter such high-opportunity fields relative to internal expansion.

Access to new technologies appears to be an important motivation underlying both acquisitions of and alliances with developing biotechnology firms by established pharmaceutical firms. One of the most important acquisitions of this genre was Hoffman-LaRoche's purchase of a large equity stake in the premier biotech firm Genentech in 1990. As a result of this deal, Hoffman-LaRoche gained access to several pioneering products being developed in Genentech's US laboratories and introduced or co-introduced several of these products into worldwide markets. In 2009, Roche acquired all the remaining outstanding shares in Genentech and moved to integrate Genentech's R&D laboratories and operations into its own international network. Other major acquisitions of biotech companies by pharmaceutical firms in 2008–2009 included the acquisition of Imclone by Eli Lilly, MGI Pharma by Esai, and Millennium by Takeda (Van Brunt 2009).

A company's desire to gain access to new technologies and areas of research also can be part of a strategic response to company-specific shocks such as aging product portfolios and future patent expirations (i.e., a combination of push and pull incentives). For example, when Glaxo acquired Burroughs-Wellcome in 1995,

it acquired an R&D-oriented company with strong research expertise in antivirals that included pioneering discoveries in the treatment of herpes and AIDS. Glaxo was also facing patent expiration for Zantac, the top-selling pharmaceutical product at that time. Correspondingly, one of the cited motives for Pfizer's merger with Wyeth was the latter's expertise in biologics, which included its prior acquisition of Immunex and its leading biological product for rheumatoid arthritis, Embrel. Pfizer is also facing the upcoming patent expiration of Lipitor, the anti-cholesterol statin drug that is currently the world's largest-selling drug product. A cardiovascular product that Pfizer hoped would affect a substantial part of Lipitor's expected lost revenues, torcetapib, was discontinued in late-stage clinical trials because of safety reasons after the company had invested almost \$1 billion in R&D expenditures (Berenson 2006).

### **Expansion to Foreign Markets and Other Stages of the Distribution Chain**

One notable type of merger that is present in the pharmaceutical industry is the cross-border merger. Some prominent examples in Table 18.1 are Pharmacia-Upjohn, SmithKline-Beecham, and Astra-Zeneca. A benefit of these mergers is an increased ability to do global launches of new products and to use the sales forces of each firm to expedite a new product's uptake and revenues. This attribute became increasingly important as generic competition intensified and product life cycles shortened in the pharmaceutical industry. Cross-border mergers have exhibited significant positive gains in event studies of market valuation (Ravenscraft and Long 2000). However, the integration process associated with different global headquarters and corporate cultures has created substantial challenges and above-average implementation costs for many of these mergers (Belcher and Nail 2000).

The M&A waves in pharmaceuticals also led to expansion downstream in the pharmaceutical distribution chain. In the 1990s, three pharmaceutical firms acquired leading PBMs. The first of these was Merck's acquisition of Medco, followed by Lilly's acquisition of PCS and SmithKline-Beecham's purchase of Diversified (Ravenscraft and Long 2000). A broad strategic rationale was to obtain an increased capacity to integrate patient claim information with pharmaceutical data to better design disease management programs and work more closely with providers on drug compliance and utilization. A number of options to bundle services seemed feasible with these PBMs.

Despite their hypothesized benefits, however, the companies undertaking vertical mergers involving PBMs exhibited significant losses in market value in the event study by Ravenscraft and Long (2000). From the start, these mergers faced antitrust issues because of the possibility that firms with PBMs could give favorable treatment to their own products on managed formularies. The pharmaceutical firms involved had to agree to organizational firewalls and other restrictions.

These controversial mergers were faced with many challenges and never really succeeded in obtaining their hoped-for strategic benefits. Subsequently, all three of the PBMs owned by pharmaceutical firms were spun off, usually with a loss write-off of significant magnitude. However, alliances between pharmaceutical firms and PBMs involving disease management programs for indications such as diabetes and asthma are still ongoing and evolving in terms of their scale and scope (Matheson et al. 2006).

## Increasing Market Power and Size

A traditional economic motive for mergers, of course, is to increase market share and market power to gain competitive advantage. This has not been a major issue in the case of the large pharmaceutical mergers depicted in Table 18.1. In the United States and elsewhere, mergers are subject to scrutiny before implementation by the antitrust authorities (Mueller 1996). There are well-known Department of Justice guidelines on what economic metrics can trigger challenges. In the case of horizontal mergers in the pharmaceutical industry, markets are usually defined in terms of therapeutic categories, because a drug product to alleviate pain, for example, does not compete with one that is approved by the Food and Drug Administration for hypertension. Therefore, horizontal mergers of significant consequence must go through a vetting process before implementation. These negotiations can result in a settlement whereby competitive products in the same therapeutic category are spun off as a condition for allowing the merger.

Whereas traditional horizontal-type mergers are constrained by the antitrust guidelines, one of the distinctive concerns for pharmaceutical M&As is in the area of innovation markets. In particular, this issue arises when two merging parties have potentially competing drug candidates in their R&D pipelines, or a new product candidate for one firm is in the same class as an already marketed product of the other firm. The concern is that this merger could result in the combined firms' suppressing a new product candidate in order to avoid cannibalizing the economic performance with the product that is carried forward or launched. The antitrust issues surrounding markets for innovation are discussed later.

Mergers may also reflect management goals to increase firm size and growth rates, even if this is not associated with increased profitability or productivity (Mueller 1986). There is a long-standing literature on the consequences of the division between ownership and management for modern corporations. One strand of this literature provides some empirical support for the fact that managerial salaries historically have been related more to size and growth in size than to profitability (Jensen and Murphy 1990; Marris 1998). However, executive compensation over recent decades has been increasingly tied to stock options and therefore to a company's market valuation and earnings performance (Hall and Liebman 1998). The evidence on M&As does not indicate that they generally increase the valuation or profitability of the surviving company (Burns et al. 2005). Despite this, managers

of firms that face a substantial downsizing due to major patent expirations may strongly prefer M&As to large-scale layoffs and the shutdown of existing facilities. Although layoffs and consolidation typically occur in the aftermath of M&As, the acquiring company can also draw on an expanded portfolio of products and pipeline candidates to maintain or increase its size.

## EFFECTS OF PHARMACEUTICAL MERGERS ON R&D AND INNOVATION

---

### Large-Scale Mergers and Subsequent Company Performance

As discussed in the previous section, there is considerable evidence that response to industry shocks has been a substantial driver of increased consolidation in pharmaceuticals. This has resulted in short-term cost savings as firms rationalize facilities and personnel, but the process is also subject to significant costs of integration. A crucial dimension of competition in a research-oriented industry like pharmaceuticals involves the ability to develop and launch significant new drug therapies. To date, however, only a handful of studies have examined the specific effects of M&As on innovative activity and R&D productivity in pharmaceuticals. As discussed later, the few studies focused on this topic have raised a number of issues and questions for further research.

Danzon et al. (2007) looked directly at the effect of mergers in pharma/biotech on various measures of performance. They focused on mergers with \$500 million or more of market value. They found that these mergers are frequently a response to distress, so it is important to compare outcomes for merging firms to outcomes for other firms with similar characteristics, and they used propensity score matching for this purpose. They concluded that mergers result in slower growth and a reduction in operating profit, although these effects are rather small. They also found smaller R&D growth for small merging firms. This does not speak to productivity directly, and the authors only looked at performance during the first three years after a merger.

Ornaghi (2006) also looked at post-merger performance in the industry but focused on productivity. He did not use the propensity score or economic distress index for developing a "control group" with which to compare the performance of merging firms. He found that in the three years following a merger, there is a decline in R&D spending as well as productivity, as measured by patents. Koenig and Mezick (2004) focused on a relatively small number of high-profile mergers consummated between 1989 and 1996 (a sample of seven large mergers). Comparing

the performance of companies in the industry that undertook these mergers with a control group of firms that did not, they found that companies that merged were able to achieve more favorable post-merger productivity scores.

A different approach and perspective was provided by Higgins and Rodriguez (2006). They focused on 160 acquisitions involving companies in the pharmaceutical and biotechnology sectors that were undertaken between 1994 and 2001. These included the purchase of many smaller biotech companies by more established pharmaceutical firms. With respect to the rationale for these acquisitions, they found that weak pipeline "scores" and fewer years of market exclusivity on launched products were primary factors for undertaking such acquisitions. Their event study analysis of outcomes found that the largest abnormal returns were realized when the acquiring firm had a prior development-stage alliance with the target firm and when both had R&D or sales experience in the same therapeutic area. This work highlighted the heterogeneity of outcomes and the possible complementary between alliances and M&As. There was also some suggestive evidence that acquiring firms were able to stabilize or reverse pipeline declines, but the authors only considered changes occurring in the first few years after an acquisition.

To summarize, there is little evidence from existing studies that M&As advance drug innovation. Although prior studies by Henderson and Cockburn (1996), Cockburn and Henderson (2001), and Danzon et al. (2005) generally identified some advantage to R&D scale and scope, the studies of major mergers suggested a weakly negative effect on R&D performance. This may be because there is no additional advantage to size at the level of most major mergers, because the integration process is disruptive to R&D progress, or because mergers are a response to distress, in which case the counterfactual is hard to determine.

Existing studies leave open many questions for further research. First, none of them looked at the long-run impact of mergers on a firm's productivity. Three years is unlikely to be enough time to pick up many changes in patenting activity, much less progression through the phases of development. Second, as Cockburn (2006) noted, patents and new chemical entities are not necessarily the best measure of output, although almost all the evidence on productivity centers on these two measures. Third, the focus has been on the larger mergers between public firms, with insufficient attention paid to heterogeneity in outcomes. The management and finance literatures are concerned with what drives a successful merger, such as whether the R&D activities of merging firms are substitutes or complements, the similarities in culture or corporate structure, the integration process, and other economic and organizational characteristics (Hitt et al. 2001). The findings of Higgins and Rodriguez (2006) on the potential benefits of prior alliances and a common R&D focus are notable in this regard and are worth examining from a longer-term perspective. Finally, the decision to merge is almost certainly endogenous, which presents an econometric challenge not fully overcome by any of the papers discussed. These issues remain important questions for future research.

## An Exploratory Study on the Effect of M&As on the Advancement of Pipeline Candidates

In a recently published study, we reported some preliminary results from a new research project that examines the effects of pharmaceutical mergers on R&D outcomes.<sup>4</sup> In contrast to other merger studies, our analysis focuses on the effects at the R&D project level of observation. R&D outcomes are measured in terms of advancement through the various phases of drug research and market launch. The study utilizes a large database of more than 4500 firms engaging in pharmaceutical R&D between 1990 and 2006. Our work is therefore closer in character to the research that has been done on alliances, which is discussed in the next section of this chapter. It includes start-up and development-stage firms with very small research programs along with the very largest multinational firms.

Our primary source for information on drug projects in development comes from IMS R&D Focus. This dataset, typically used by pharmaceutical firms to monitor the research activities of their competitors, provides a history of *all* projects known to be in development from the mid-1980s to present. This includes projects that failed in clinical trials during this period, those that were successfully launched, and those that are still in development (since projects normally take between 3 and 10 years to complete clinical trials before reaching the market).

Because most of the 4500+ firms in this data set are not publicly traded in the United States, we lack consistent time-series financial data such as firm-level R&D spending, total asset size, and other important control variables used in most other studies of mergers in this industry. Those studies have focused on the performance of large, public firms with several marketed products. Our data have the advantage of including firms of varying size, but at the cost of poorer information on financial data for nonpublic firms.

Using a firm's count of active drug development projects each year, we create four size categories: small (fewer than 5 projects underway in a year), medium (5–20 projects), large (20–50 projects), and very large (more than 50 projects) to measure firm size.<sup>5</sup> Size in this study therefore serves as a measure of the firm's experience in its clinical trial activities. The dependent variable in our analysis is the likelihood of advancement to the next stage of development, beginning in phase 1 through phases 2 and 3 to final marketing approval. We assume a five-year window for advancement; this implies some truncation for recent projects (which we observe through the first quarter of 2007), but most projects that advance do so in less than four years.

4. We use the term *mergers* in this section to encompass all M&A activity by the firms in our samples.
5. Based on the R&D Focus database from IMS, the top five companies in Table 18.1 in the latest ranking averaged more than 250 projects across the various stages of the R&D process in 2006.

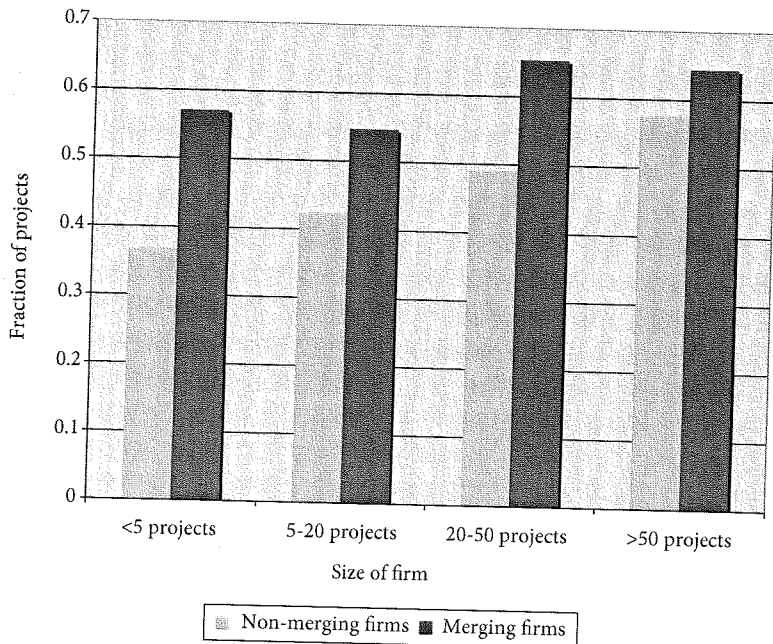


Figure 18.1 Fraction of projects advanced within 5 years, phase 3 to launch.

Our analysis finds that a higher fraction of projects of firms that experienced a merger during the 1985–2006 period progress to the next phase, compared with projects of nonmerging firms, with the most substantial differences being observed in phase 3.<sup>6</sup> Figure 18.1 shows the fraction of projects advancing from phase 3 to launch by size of firm and whether the firm engaged in a merger. For firms that did not undertake a merger, there is also a strong positive relationship between size and performance in phase 3. Using a logit regression approach to control for size, the year when a project is initiated, and whether a project was pre-merger or post-merger, we find that projects initiated after a merger are much more likely to advance from each stage of development. This suggests a benefit to merging that is independent of size alone, although econometric concerns regarding endogeneity remain.

6. When a merger occurs, IMS updates the record of a drug project with the name of the merged firm. In order to examine the performance of a firm prior to a merger, therefore, it is necessary to identify which of the merging firms originated each project that existed before the merger. To do so, we rely on patent information (because, typically, the patent assignee is the originating firm) as well as the text summary of research for each record. This text summary includes the source of information about a drug's status; if the source is one of the merging firms, we assume that the project was originated by that source. With this method, we can successfully assign about 80 percent of drug projects that began prior to a merger to one of the merging firms.

Although we refer to a higher rate of advancement as higher “performance,” this is not necessarily true. Because drug development costs increase with each stage, it is better to identify likely failures earlier rather than later. Firms that are better able to make this judgment early on in the development process may advance a lower fraction of projects in phase 1 or 2 but have a higher probability of success and of marketing approval for projects that progress to phase 3. The higher probability of success for phase 3 for the largest-scale firms is consistent with the hypothesis that they have a comparative advantage at later stages of the R&D process (Arora et al. 2001) or, alternatively, with the hypothesis that large firms are better at weeding out unlikely successes earlier in the process (Guedj and Scharfstein 2004). Further research on this issue is warranted.

An important question for further research is the source of such benefits. Do mergers combine complementary skills of two firms, leading to better project selection? Do mergers reduce potential competition within a disease area, raise expected profits for a project, and therefore lead to more advancement? Are mergers necessary for the realization of these benefits, or could strategic alliances be used instead? Are firms that enter into alliances before mergers have higher probabilities of success in their R&D projects? These are among the issues we hope to address in future research.

## ALLIANCES AS A SUBSTITUTE FOR, OR COMPLEMENT TO, MERGERS

---

### Rationales for Alliances

As discussed in first section of this chapter, larger firms are also increasingly looking to alliances and partnerships with smaller biotechnology firms as the source of new products. This can be viewed as another strategic response to industry shocks as well as a proactive motivation to gain access to new technologies. In particular, alliances allow larger firms to buttress pipelines in anticipation of future patent expirations. A prototypical development-stage agreement would involve payments of milestones and/or royalties and some sharing of R&D expenses in exchange for rights to develop and/or market the new products covered under the agreement. The extent of integration at the R&D stage associated with these agreements varies considerably, ranging from true joint development agreements, to transfers of development-stage products from licensors to licensees, to securing of marketing options in exchange for development-stage funding and future payments.

Another rationale for alliances is R&D specialization based on comparative advantages in research versus development. This argument was advanced by

Kenneth Arrow (1983) in a more general model of the R&D process. At the early stages of R&D, small, research-oriented boutique firms may enjoy a number of advantages relative to their larger rivals. These include their proximity to cutting-edge technology emerging from universities and publicly supported basic research, willingness to take risks on disruptive technologies, and less bureaucratic organizational structure (Scherer 1999). By contrast, larger pharmaceutical and biotechnology firms may have advantages in the more advanced stages of development, when large-scale clinical trial design and regulatory coordination become important (Food and Drug Administration 1999.)

Whereas alliances and partnerships are an alternative to mergers as a means to acquire new technological platforms and R&D pipeline candidates, they also pose their own set of issues. Arora et al. (2001) found support for gains from a division of labor at alternative stages of the R&D process. There also are positive network effects associated with alliances and partnerships (Powell et al. 1996; Pammolli and Riccaboni 2004). On the other hand, partnership deals may be susceptible to a "lemons" problem arising from agency and information problems (Akerlof 1970; Pisano 1997). Partnerships also raise challenging bargaining, management, and governance issues (Teece 1998; Arora et al. 2001).

Many M&As in the pharmaceutical area have occurred between firms that had first engaged in some type of alliance or partnership (Higgins and Rodriguez 2006). Such arrangements may help merging firms overcome pitfalls associated with agency problems and information asymmetries. In particular, the information gathered over time from an alliance may allow the acquiring firm to better assess the value of the acquired firm's intangible capital. It may also provide information on the resulting organization's ability to successfully integrate the strengths of the two companies. The difficulty of integrating firms with different cultures and organizational structures is an oft-cited reason for failures of mergers in the management literature (Haspeslagh and Jemison 1991; Smith and Quella 1995; Larsson and Finkelstein 1999). Firms that have engaged in prior alliances have teams of individuals that know each other and have collaborated on projects, lessening the potential problems of integration that plague many M&As. There is at least some preliminary evidence consistent with these hypothesized benefits from alliances. Higgins and Rodriguez (2006) found that acquisitions involving alliance partners had higher abnormal stock market returns than did firms with no prior history of alliances.

## Effects of Alliances on R&D and Innovation

The most extensive published study evaluating the performance of alliances is that of Danzon et al. (2005). They examined the productivity at each phase of drug development (i.e., success probabilities) for 900 firms over the period 1988– to 2000. In looking at economies of scale, they focused on experience (measured by the number of drugs a firm has in development) rather than sales.

They found that the effect of experience on productivity (i.e., advancing a drug through a phase of clinical trials) was positive, with diminishing returns for phases 2 and 3, and with the maximum occurring with 25 drugs in development. Products developed in an alliance tended to have a higher probability of success, at least for phase 2 and 3 trials, and especially when the licensee was a large firm.

Arora et al. (2007) also examined the role of licensing and alliances, using data from 3,000 R&D projects in preclinical and clinical trials in the United States in the 1980s and 1990s. After controlling for selection effects, they found that licensing improves the probability of success when the licensee is a pharmaceutical firm. Their results were therefore generally similar to those of Danzon et al. (2005) on the positive benefits of alliances. Both studies were inconsistent with the "lemons" hypothesis put forward by Pisano (1997), at least for typical development-oriented licensing arrangements between biotech and advanced pharmaceutical firms; however, neither study tested for asymmetric information directly.

In contrast to the work on large-scale mergers, studies of alliances have found more positive effects on R&D performance. In these studies, development experience was generally associated with higher success probabilities, especially in later R&D stages. Hence, there appears to be a potentially important role for specialization across R&D stages. An advantage of these studies is that they were performed with R&D project-level data, including a large number of observations spanning a large spectrum of firm sizes and prior experiences in R&D.

These leading studies on the effects of alliances and innovation also raise many issues for further research. The business alliance literature suggests a rich array of contractual terms and an evolving landscape of ventures. In this regard, Danzon et al. (2005) did not explicitly consider the contractual terms, the extent of integration of the R&D process, or the characteristics of the firms involved in the agreement beyond a few simple attributes relating to a firm's size and experience in performing clinical trials. Arora et al. (2007) adjusted for product selection effects, but their analysis considered only a few characteristics variables. Both studies raised a number of issues about the underlying drivers of successful alliances for further research analysis. As in the study of M&As, greater attention to the heterogeneity of outcomes and the affects of various economic and organizational characteristics on these outcomes seems warranted.

## Market Structure and the Incentives for Efficient Alliances

A study by Allain et al. (2009) combined a theoretical model with empirical evidence to examine how market structure influences the incentives for firms to undertake alliances and realize good outcomes. Building on the alliance literature discussed earlier, their model assumed that biotechnology firms, or

licensors, have private information about the quality of their drug candidates but are less efficient at drug development than are large pharmaceutical firms. This asymmetric information undermines the market for technology: because of the potential for a lemons market, pharma firms offer prices for licenses based on the expected quality of an innovation, and these prices are too low for good innovations. A study by Nicholson et al. (2005) confirmed this result. Biotech firms with good innovations will therefore choose to perform clinical trials themselves, even though this is inefficient, in order to prove their quality and command a higher price for a license later on. Competition among pharmaceutical firms for the innovation has two effects on the delay associated with licensing. First, competition drives up the price for a license that a biotech firm with a good innovation can expect from waiting to license, which has the effect of increasing delay. In other words, competition for the license can increase inefficient delays in the market for technology, which is an effect not considered in other papers. But competition has a countervailing effect as well if the firms competing for the license also compete on the product market. Intense downstream competition erodes the profits that can be derived from the innovation, giving a biotech firm less reason to delay licensing. The authors found evidence for both effects of competition using data on the stage of development at which licenses were signed during 1990–2006.

## ANTITRUST POLICY CONSIDERATIONS

---

### Innovation Markets

The idea that antitrust authorities should concentrate on innovation markets in research-intensive industries such as pharmaceuticals was first advanced in the economics literature in a paper by Gilbert and Sunshine (1995). The key issues revolve around potential competition from products in the merging firms' R&D pipelines. To date, there have been 10 challenges to mergers in innovation markets, and 8 of these have involved the pharmaceutical industry (Carrier 2008). The lengthy and costly R&D process (DiMasi et al. 2003) and the high potential economic barriers to developing new products and gaining regulatory approval have made pharmaceuticals a area of particular scrutiny.

Although the concept of innovation markets has its supporters in antitrust enforcement, its applications have been criticized by many economists and lawyers (Carlton 1995; Rapp 1995; Carrier 2008). For pharmaceuticals, with their long and uncertain development process, critics argue that antitrust authorities should focus on drug candidates in the late stage of development, where potential

competition is more easily assessed. Early-stage development activities involve relatively low costs and barriers to entry and are also subject to high levels of uncertainty.<sup>7</sup> Many firms take a portfolio approach to obtaining new product introductions at the early stages of R&D. There are also typically many parallel R&D efforts across firms searching for promising new therapeutic approaches (DiMasi and Pacquette 2004). When a drug progresses to the final phase 3 of clinical testing, however, the probability of success increases to approximately 70 percent, and costs of clinical trials also increase significantly (DiMasi et al. 2003). Traditional antitrust concerns about potential competition effects then become more relevant, particularly when there are a small number of late-stage competitors for these product candidates.

Carrier (2008) performed an analysis of each of the eight innovative market cases in pharmaceuticals. He found that some of the challenges by the antitrust authorities were warranted, but others were more problematic given the relevant characteristics of the market and an analysis of the potential costs and benefits. In the questionable cases, he argued that the Federal Trade Commission (FTC) attempted to protect innovation when future outcomes were uncertain and many years away from the market. By contrast, the European Union has taken a less stringent approach to some of these innovation market cases (Morgan 2001). This is clearly an evolving area of antitrust policy that warrants more research and attention by scholars.

## Potential Adverse Effects of Large Mergers on Alliances With Earlier-Stage Companies

As discussed previously, antitrust policy toward mergers has focused on the extent to which merging firms sell products in the same therapeutic area, and more recently on potential overlap in pipelines or “innovation markets.” Two former Directors of the Bureau of Economics of the FTC, William Comanor and F. M. Scherer, co-authored a memorandum to the FTC raising additional concerns that the Commission should consider in reviewing large-scale mergers (Comanor and Scherer 2009). In particular, they emphasized the important role that early-stage development biopharmaceutical firms have played in originating new chemical and biological entities in recent years and the importance of multiple parallel paths to new drug discovery and development in an R&D process that is subject to high levels of uncertainty.

Whereas private equity firms are key funding sources at the earliest stages of the technology transfer process, partnerships and acquisitions are important

7. More than 75 percent of the drugs entering phase 1 fail to reach the market for safety, efficacy, or competitive reasons (DiMasi et al. 2003).

funding sources as products move beyond proof of concept into expensive clinical trials to gain regulatory approval. The R&D process is long, costly, and risky. It typically takes a decade or longer from initial synthesis to regulatory approval, and only about one-quarter of the drugs that begin clinical trials become marketed drugs. Most venture capital partnerships have a lifetime of only 10 years and have restrictions that prohibit concentration of a large share of their portfolio in any one company. Hence, partnerships often become essential to the advancement of these early-stage companies.

Given these facts, Comanor and Scherer (2009) suggested several concerns that antitrust officials should address in evaluating mergers between firms with large sales even if there are no significant overlaps in the particular therapeutic areas of each firm. First, they pointed out that these large-scale mergers reduce the cohort of independent firms that are available to partner with or acquire earlier-stage biopharmaceutical firms. This can lead to progression of fewer projects originating in early-stage biopharmaceutical firms into later stages of the R&D process along parallel paths. Furthermore, the attendant reduction of R&D facilities and resources accompanying mergers is likely to reduce the number of internally originated projects compared to what would occur with two separate R&D-oriented firms. They were skeptical that these mergers could produce any offsetting benefits from economies of scale or scope in R&D, given the evidence from the available literature.

Although these issues and concerns did not prevent the FTC approval of large-scale mergers such as Pfizer-Wyeth or Merck-ScheringPlough in 2009, they raise interesting questions for further research. In particular, even if mergers between large firms reduce overall R&D expenditures and the number of projects undertaken, it is important to understand the balance of impacts between internally generated projects and externally supported ones. It may be that internal projects bear the brunt of these cutbacks when firms are integrated. If many marginal internal projects are eliminated, this may leave the door open for more outside partnership opportunities.

Second, it is important to know the effects on early-stage versus later-stage development projects and firms. At present, there appears to be a strong demand for late-stage product candidates, with substantial market potential to fill pipeline gaps, so adverse effects, if any, may be seen primarily with deals for early-stage companies. This has traditionally been the forté of venture capital companies rather than established biopharmaceutical companies. But there is evidence that venture capitalists have pulled back their support of early-stage research-oriented companies in the wake of the NASDAQ market bubble and worldwide financial problems in recent years. This has left a funding gap in the technology transfer development process for start-ups with technologies that have proceeded beyond university-type basic research but still are many years away from any commercial applications. This area could use some creative funding approaches and new organizational structures, as has been suggested by some industry observers (Klausner 2005).

## SUMMARY AND CONCLUDING COMMENTS

---

As is the case in other industries, mergers in the pharmaceutical field are driven by a variety of company motives and conditions. These include defensive responses to industry shocks as well as more proactive rationales, such as economies of scale and scope, access to new technologies, and expansion to new markets. It is important to take account of firms' characteristics and motivations in evaluating merger performance, rather than using a broad aggregate brushstroke. Research to date on pharmaceuticals suggests considerable variation in both motivation and outcomes.

The empirical research on mergers has generally focused on the larger public companies. There is evidence that the mergers involving these pharmaceutical firms were driven in significant part by a series of industry-wide and firm-specific shocks which left many firms with R&D pipeline gaps associated with patent expirations and increased generic competition. These mergers have had mixed success in addressing these short-run pipeline problems. However, there is little evidence to date that they have increased long-term R&D performance or outcomes. Many of the larger pharmaceutical firms listed in Table 18.1 continue to deal with a persistent R&D productivity problem.

By contrast, the empirical research on alliances between smaller biotech firms and larger pharmaceutical entities suggests a role for small- and large-firm specialization at different R&D stages. There is evidence of a positive relation between a firm's experience in clinical development and the probability of successful outcomes. This suggests that "R&D boutique" firms with a small number of research projects can benefit from alliances with larger, more experienced firms, especially at the later stages of the R&D process. Our own analysis of the effect of mergers on R&D project advancement by stages is generally consistent with these results from the alliance literature. We find that very small firms with only a few projects in their R&D portfolio can gain the most benefit from M&As by firms that are more experienced in development of new drug candidates. The work of Higgins and Rodriguez (2006) also indicates that prior alliances can help firms overcome asymmetric information and integration problems frequently associated with acquisitions in the pharmaceutical industry.

The results of all of the studies on M&As and alliances are subject to various caveats about interpretation and raise many questions for further research. These include the choice of output measures, sample coverage, and time frames and the endogenous relationships between motives and outcomes. More generally, there are a host of interesting research questions to be addressed relating to the heterogeneity of effects and the conditions and firm characteristics that produce successful versus unsuccessful outcomes. It is also important to understand when alliances are a desirable alternative to mergers and when they can be complementary in nature. These are important issues from the standpoints of both business strategy and economic efficiency.

From an antitrust policy standpoint, the larger horizontal mergers in pharmaceuticals have run into few challenges from regulatory authorities in the United States and the European Union, given the option to spin off competing therapeutic products to other drug firms. However, the issue of innovation markets, where firms have potentially competing development programs at very early stages of the R&D process, remains a more controversial area of antitrust policy for industries like pharmaceuticals. The potential adverse effects of large-scale mergers in reducing partnering opportunities for development-stage companies is another dimension of innovation markets recently raised by economists for consideration by antitrust authorities. Research into the effects of mergers on innovation markets remains an important topic for law and economics scholars.

## REFERENCES

- Akerlof, G.A. 1970. "The Market for 'Lemons': Quality Uncertainty and the Market Mechanism." *Quarterly Journal of Economics* 84: 488–500.
- Allain, M.-L., E. Henry, and M. Kyle. 2009. "The Timing of Licensing: Theory and Empirics." Unpublished paper. Available from the authors.
- Andrade, G., M. Mitchell, and E. Stafford. 2001. "New Evidence and Perspectives on Mergers." *Journal of Economic Perspectives* 15(2): 103–120.
- Arora, A., A. Fosfuri, and A. Gambardella. 2001. *Markets for Technology: The Economics of Innovation and Corporate Strategy*. Cambridge, MA: MIT Press.
- Arora, A., A. Gambardella, L. Magazzini, and F. Pammolli. 2007. "A Breath of Fresh Air? Firm Types, Scale, Scope and Selection Effects in Drug Development." Unpublished paper. Available from the authors.
- Arrow, K.J. 1983. "Innovation in Large and Small Firms." In *Entrepreneurship*, ed. J. Ronen. Lexington, MA: Lexington Books.
- Belcher, T., and L. Nail. 2000. "Integration Problems and Turnaround Strategies in a Cross-border Merger: A Clinical Examination of the Pharmacia-Upjohn Merger." *International Review of Financial Analysis* 9(2): 219–234.
- Berenson, A. 2006. "End of Drug Trial Is Big Loss for Pfizer," *New York Times*, December 4. Available at <http://www.nytimes.com/2006/12/04/health/04pfizer.html?scp=1&sq=&st=nyt> (accessed November 2011).
- Berndt, E.R., and M.L. Aitken. 2010. "Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation." National Bureau of Economic Research Working Paper 16431.
- Burns, L.R., S. Nicholson, and J. Evans. 2005. "Mergers, Acquisitions and the Advantages of Scale in the Pharmaceutical Industry." In *The Business of Healthcare*, ed. L.R. Burns, 223–270. Cambridge: Cambridge University Press.
- Carlton, D.W. 1995. *Antitrust Policy Towards Mergers When Firms Innovate: Should Antitrust Recognize the Doctrine of Innovation Markets?* Testimony before the Federal Trade Commission on Hearings on Global and Innovation-Based Competition. Available at <http://www.ftc.gov/opp/global/carlton.htm> (accessed November 2011).
- Carrier, M.J. 2008. "Two Puzzles Resolved: Of the Schumpeter-Arrow Stalemate and Pharmaceutical Innovation Markets." *Iowa Law Review* 93. Available at <http://ssrn.com/abstract=977603> (accessed November 2011).

- Centerwatch. 2000. "Some Troubling Numbers for Big Pharma Consolidation." *In Vivo* (July/August): 18(7): 2-3.
- Clark, I. 2001, December. "Drug Discovery: Resolving the Bottlenecks." *Horizons*, Pharmaceutical Issue 1.
- Cockburn, I. 2006. "Is the Pharmaceutical Industry in a Productivity Crisis?" In *Innovation Policy and the Economy*, eds. A. Jaffe, J. Lerner, and S. Stern, 1-32. Cambridge, MA: MIT Press.
- Cockburn, I., and R. Henderson. 2001. "Scale and Scope in Drug Development: Unpacking the Advantages of Size in Pharmaceutical Research." *Journal of Health Economics* 20(6): 1033-1057.
- Comanor, W.S. and F. M. Scherer. 2009. "Comments Submitted to the Federal Trade Commission on the Pfizer Wyeth and Merck-Schering Plough Mergers." Available at <http://www.ftc.gov/os/comments/pfizerwyeth/544915-00004.pdf> (accessed November 2011).
- Danzon, P., A. Epstein, and S. Nicholson. 2007. "Mergers and Acquisitions in the Pharmaceutical and Biotech Industries." *Managerial and Decision Economics* 28(4/5): 307-328.
- Danzon, P., S. Nicholson, and N.S. Pereira. 2005. "Productivity in Pharmaceutical-Biotechnology R&D: The Role of Experience and Alliances." *Journal of Health Economics* 24(2): 317-339.
- DiMasi, J., and H. Grabowski. 2007. "The Economics of New Oncology Drug Development." *Journal of Clinical Oncology* 25(2): 209-216.
- DiMasi, J., R. Hansen, and H. Grabowski. 2003. "The Price of Innovation: New Estimates of Drug Development Costs." *Journal of Health Economics* 22: 141-185.
- DiMasi, J., and C. Pacquette. 2004. "The Economics of Follow-on Drug Research and Development: Trends in Entry Rates and the Timing of Development." *PharmacoEconomics* 22(Suppl. 2): 1-14.
- Dorey, E. 2001. "GlaxoSmithKline Present a Biotech Facade." *Nature Biotechnology* 19(4): 294-295.
- Ernst and Young Online. 2011. *Beyond Borders: Global Biotechnology Report 2007*. Available at <http://www.ey.com/beyondborders> (accessed November 2011).
- Gilbert, R.J., and S.C. Sunshine. 1995. "Incorporating Dynamic Efficiency Concerns in Merger Analysis: The Use of Innovation Markets." *Antitrust Law Journal* 63: 569-602.
- Gort, M. 1969. "An Economic Disturbance Theory of Mergers." *Quarterly Journal of Economics* 83: 624-642.
- Grabowski, H. 2007. "Competition Between Generic and Branded Drugs." In *Pharmaceutical Innovation: Incentives, Competition, and Cost-Benefit Analysis in International Perspective*, eds. F.A. Sloan and C.-R. Heish, 153-173. Cambridge, UK: Cambridge University Press.
- Grabowski, H., J. Vernon, and J. DiMasi. 2002. "Returns on Research and Development for 1990s New Drug Introductions." *PharmacoEconomics* 20(Suppl. 3): 11-29.
- Guedj, I., and D. Scharfstein. 2004. "Organizational Scope and Investment: Evidence from the Drug Development Strategies and Performance of Biopharmaceutical Firms." NBER Working Paper 10933. Cambridge, MA: National Bureau of Economic Research.
- Hall, B.J., and J.B. Liebman. 1998. "Are CEOs Really Paid Like Bureaucrats?" *Quarterly Journal of Economics* 113(3): 653-691.
- Haspeslagh, P., and D. Jemison. 1991. *Managing Acquisitions: Creating Value Through Corporate Renewal*. New York: Free Press.

- Henderson, R., and I. Cockburn. 1996. "Scale, Scope, and Spillovers: Determinants of Research Productivity in the Pharmaceutical Industry." *RAND Journal of Economics* 27(1): 32-59.
- Higgins, M.J., and D. Rodriguez. 2006. "The Outsourcing of R&D Through Acquisition in the Pharmaceutical Industry." *Journal of Financial Economics* 80: 351-383.
- Hitt, M., R.D. Ireland, and J. Harrison. 2001. "Mergers and Acquisitions: A Value Creating or Value Destroying Strategy?" In *The Blackwell Handbook of Strategic Management*, eds. M. Hitt, R.E. Freeman, and J. Harrison, 384-408. Malden, MA: Blackwell Business.
- Jensen, M.C., and K. Murphy. 1990. "Performance Pay and Top Management Incentives." *Journal of Political Economy* 98(2): 225-265.
- Klausner, A. 2005. "Mind the (Biomedical Funding) Gap." *Nature Biotechnology* 23: 1217-1218.
- Koenig, M., and E. Mezick. 2004. "Impact of Mergers and Acquisitions on Research Productivity Within the Pharmaceutical Industry." *Scientometrics* 59(1): 157-169.
- Larsson, R., and S. Finkelstein. 1999. "Integrating Strategic, Organizational, and Human Resource Perspectives on Mergers and Acquisitions: A Case Survey of Synergy Realization." *Organization Science* 10(1): 1-26.
- Marris, R. 1998. *Managerial Capitalism in Retrospect*. New York: St. Martin's Press.
- Matheson, D., A. Wilkins, and D. Psacharopoul. 2006. *Realizing the Promise of Disease Management*. Boston, MA: Boston Consulting Group.
- Mathieu, M., ed. 2007. *Parexel's Bio/Pharmaceutical R&D Scoreboard 2007/2008*. Waltham, MA: Parexel International Corporation.
- Morgan, E.J. 2001. "Innovation and Merger Decisions in the Pharmaceutical Industry." *Review of Industrial Organization* 19: 181-197.
- Mueller, D.C. 1986. *The Modern Corporation Profits, Power Growth and Performance*, Sussex, UK: Wheatsheaf Books.
- Mueller, D.C. 1996. "Lessons from the United States' Antitrust History." *International Journal of Industrial Organization* 14: 415-445.
- Nicholson, S., P. Danzon, and J. McCullough. 2005. "Biotech-Pharmaceutical Alliances as a Signal of Asset and Firm Quality." *Journal of Business* 78(4): 1433-1464.
- Ornaghi, C. 2006. *Mergers and Innovation: The Case of the Pharmaceutical Industry*. Discussion Papers in Economics and Econometrics 0605. Southampton, UK: University of Southampton.
- Pammolli, F., and M. Riccaboni. 2004. "Technological Competencies in Networks of Innovators." In *The Economics and Management of Technological Diversification*, eds. J. Cantwell, A. Gambardella, and O. Grandstrand. London and New York: Routledge.
- Pisano, G. 1997. "R&D Performance, Collaborative Arrangements, and the Market for Know-How: A Test of the 'Lemons' Hypothesis in Biotechnology." Mimeo. Cambridge, MA: Harvard Business School.
- Powell, W., K. Koput, and L. Smith-Doerr. 1996. "Interorganizational Collaboration and the Locus of Innovation: Networks of Learning in Biotechnology." *Administrative Science Quarterly* 41: 116-145.
- Rapp, R.T. 1995. "The Misapplication of the Innovation Market Approach to Merger Analysis." *Antitrust Law Journal* 64: 19-47.
- Ravenscraft, D.J., and W.F. Long. 2000. "Paths to Creating Value in Pharmaceutical Mergers." In *Mergers and Productivity*, ed. S.N. Kaplan. Chicago: University of Chicago Press.

- Recombinant Capital. 2008. "Analysts Notebook: Trends." Available at <http://www.recap.com/consulting.nsf/ContentWebPublish/9A5A93B5D9B4080A882574440076AB44.001?OpenDocument> (accessed January 16, 2012).
- Scherer, F.M. 1999. *New Perspectives on Economic Growth and Technological Innovation*, Washington, DC: The Brookings Institution.
- Smith, K., and J. Quella. 1995. "Seizing the Moment to Capture Value in a Strategic Deal." *Mergers and Acquisitions* 29(4): 25-30.
- Teece, D.J. 1998. "Capturing Value From Knowledge Assets: The New Economy, Markets for Know-How and Intangible Assets." *California Management Review* 40(3): 55-79.
- Food and Drug Administration, Center for Drug Evaluation and Research. 1999. *From Test Tube to Patient: Improving Health Through Human Drugs* [Special report]. Washington, DC: US Government Printing Office.
- Van Brunt, J. 2009. "Shuffling the Deck—Again." *Signals Magazine: Focal Point* 11/19/2009. Available at <http://www.signalsmag.com> in the Contents Archive (accessed November 2011).