THE EFFECTS OF CORE BUSINESS DIVESTMENTS ON INNOVATIONS WITHIN THE PHARMACEUTICAL INDUSTRY: A PUBLIC POLICY ANALYSIS

by

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The Effects of Core Business Divestments on Innovations within the Pharmaceutical Industry: A Public Policy Analysis

A Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at George Mason University

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DEDICATION

This is dedicated to the friends who supported me during the process, especially to my mentor Frank Hearl who was always understanding and encouraging of this pursuit.
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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>List of Tables</th>
<th>vii</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Figures</td>
<td>viii</td>
</tr>
<tr>
<td>Abstract</td>
<td>ix</td>
</tr>
</tbody>
</table>

## chapter One: Introduction

1.01 Overview: Divestment as a reaction to patent expirations ........................................ 1
1.02 Current Trends: Background ................................................................................... 4
1.03 Background on divestments .................................................................................... 6
1.04 The literature on divestments and innovations across industries ....................... 9
1.05 The literature on divestments and innovations within the pharmaceutical industry .......................................................................................................................... 11
1.06 Research Proposal ................................................................................................. 12
1.07 Public policy implications ...................................................................................... 14
1.08 Contribution of this study ..................................................................................... 16
1.09 A note about the pharmaceutical industry ........................................................... 17
1.10 Firms changed capabilities to seek outside knowledge ........................................ 23
1.11 FDA Drug Approval Process .................................................................................. 26

## Chapter two: theory development

2.01 Resource based view and capabilities perspective ................................................. 31
2.02 Knowledge Brokering ......................................................................................... 33
2.03 Knowledge brokering capabilities ......................................................................... 34
2.04 Absorptive capabilities ....................................................................................... 35
2.05 Managerial capabilities ....................................................................................... 37
2.06 Divestment capabilities ....................................................................................... 40
2.07 Innovations theory ............................................................................................... 42
2.08 The impact of regulations on innovations ............................................................ 45
<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1 Major legislation</td>
<td>49</td>
</tr>
<tr>
<td>Table 2 Summary statistics of the variables</td>
<td>75</td>
</tr>
<tr>
<td>Table 3 Correlations</td>
<td>76</td>
</tr>
<tr>
<td>Table 4 Regression results and post estimation tests</td>
<td>77</td>
</tr>
<tr>
<td>Table 5 Firms with top betweenness centrality scores</td>
<td>81</td>
</tr>
<tr>
<td>Table 6 Firms with top betweenness centrality scores before 1993</td>
<td>98</td>
</tr>
<tr>
<td>Table 7 Firms with top betweenness centrality scores after 1993</td>
<td>101</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>1</td>
<td>Drug development process</td>
</tr>
<tr>
<td>2</td>
<td>Theoretical model of the effect of core divestments</td>
</tr>
<tr>
<td>3</td>
<td>Theoretical model of the effect of divestments moderated by knowledge brokering</td>
</tr>
<tr>
<td>4</td>
<td>Network analysis of entire network using betweenness centrality</td>
</tr>
<tr>
<td>5</td>
<td>Network analysis of central firms using betweenness centrality</td>
</tr>
<tr>
<td>6</td>
<td>Divestment network before 1993</td>
</tr>
<tr>
<td>7</td>
<td>Divestment network of central firms before 1993</td>
</tr>
<tr>
<td>8</td>
<td>Divestment network after 1993</td>
</tr>
<tr>
<td>9</td>
<td>Divestment network of central firms after 1993</td>
</tr>
</tbody>
</table>
ABSTRACT

THE EFFECTS OF CORE BUSINESS DIVESTMENTS ON INNOVATIONS WITHIN THE PHARMACEUTICAL INDUSTRY: A PUBLIC POLICY ANALYSIS

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George Mason University, 2014

Dissertation Director: Dr. Sonia Ketkar

A report by the Financial Times estimated that global divestments would increase by 90 percent and grow to become a 250 pound sterling industry ("The Cost of Pharma Divorce," 2012). Studying divestments in the pharmaceutical industry is critical because divestments can negatively impact innovations. Pharmaceuticals companies today are undertaking divestment of core as opposed to non-core business activities. Our research questions are: (i) what is the effect of core divestment on innovation and (ii) do knowledge brokering capabilities moderate this relationship? And what are the public policy implications? Thus, in this study, we theoretically introduce and empirically explore the construct ‘knowledge brokering’ and examine its role in the relationship between divestment and innovation in the pharmaceuticals industry. Large
pharmaceutical firms are strategically divesting to transform themselves from knowledge producers into “knowledge brokers” (Gassmann and Reepmeyer, 2005).

In the pharmaceutical industry, each new generation of products finances the R&D of the next generation of drug candidates. A failure to innovate imposes penalties against future R&D investments (Kaitin, 2010). For this reason, a steady stream of innovations is especially important to public health and public policy. Pharmaceutical companies are divesting, in some cases, as a reaction to patent expirations (the loss of patent protection) but they are not exiting from the business of producing innovations (Kester, 2009).

Our results suggest that the pharmaceutical industry is moving away from the traditional business model of producing knowledge in-house to producing innovations via knowledge brokers in networks. In some cases, the industry’s reaction to expiring patents is to externalize R&D risk via core divestments. Externalization of risk means shifting in-house risk to external entities. The new business model relies more on sourcing knowledge from outside of the firm within knowledge networks. This move to a different business model is an adaptive strategy for firm survival that reflects the collaborative nature of contemporary scientific research (Gassmann & Reepmeyer, 2005). Firms need to successfully absorb information from the outside scientific environment.

Knowledge brokering via divestments is a way that large brand-name pharmaceutical companies can simultaneously exploit their managerial capabilities and
absorptive capabilities. There is always a tension between exploration and exploitation for firms. Exploration is looking for new things to do and new ways of doing them. Exploitation is continuing to do what firms already know how to do (Duane Ireland & Webb, 2007). Divesting core business via knowledge brokering is a way to explore emerging scientific opportunities while exploiting what large firms do well, which is managing the complicated FDA approval process. As long as pharmaceutical companies produce innovations, sourcing knowledge from outside of the firm benefits public health.
1.01 Overview: Divestment as a reaction to patent expirations

The pharmaceutical industry is a highly regulated industry that makes strategic business decisions based on public policy: regulation and legislation (Hamburg, 2010; Hong, Shepherd, Scoones, & Wan, 2005; Kesselheim, 2011). As the largest market for pharmaceuticals, the U.S. carries the most regulatory sway in that firms weigh U.S. regulation and legislation heavily when making business decisions (Archibugi & Filippetti, 2010). One important type of legislation is patent law. Studies have shown that decisions by pharmaceutical companies to merge, acquire and divest can be reactions to patent expirations. These transactions can involve core or noncore business (Bouchard, 2007; Kesselheim, Murtagh, & Mello, 2011; Kesselheim, 2011). For instance, brand-name pharmaceutical companies grew through mergers and acquisitions in an attempt to avoid the “patent cliff” or when the most profitable patents expire and there are no comparable patents to replace them. With soon-to-expire patents and no new patents in the pipeline, pharmaceutical companies merged with or acquired other firms that held patents with greater longevity in order to infuse cash (Kaitin & DiMasi, 2010). This study argues that the spate of current divestments is likely a reaction to patent expirations and the regulatory environment, in which medicines only enjoy a small
fraction of the 20-year patent protection because developing a drug to meet regulatory standards is time consuming (Danzan & Keuffel, 2013). Note that we do not claim all divestments are a reaction to patent expirations. We will analyze firm behavior within the context of public policies related to patents and FDA approval.

Divestments of core business include both externalization of R&D and the sale of entire divisions of disease areas (Kaitin & DiMasi, 2010; Paul et al., 2010). A report by the Financial Times estimated that global divestments would increase by 90 percent and grow to become a 250 billion pound sterling industry (or 397 billion USD) (“The Cost of Pharma Divorce,” 2012). Among a sampling frame of 190 pharmaceutical firms, from 1997 to 2006, there were over 100 divestments per year. In 1997, only 18.4 percent of firms divested whereas in 2006, 27.9 percent of firms divested. Examples of the magnitude of divestment deals are those of Novartis worth 5.4 billion pounds sterling (8.59 billion USD) and Bayer AG worth 4.5 billion pounds sterling (7.16 billion USD) in 2007 (Kester, 2009).

One can argue that the current spate of divestments is simply a result of over-diversified firms that are now selling unrelated units to focus on their core competencies. This trend was evident in the 1980s and 1990s (Pettigrew, Thomas, & Whittington, 2006). However, the recent divestments might be different due to their sale of core, related businesses and not only non-core units (Kester, 2009). The core business of large brand-name pharmaceutical companies is researching and developing innovative drugs for human consumption. The core business of large brand-name
pharmaceutical companies is important because they house the companies’ core capabilities. For this research-intensive industry, R&D is the engine that has traditionally driven innovations (Kester, 2009).

There are synergies to a pharmaceutical company having a broad research portfolio due to economies of scale and because discoveries are often serendipitous events that are discovered during cross-fertilization between different research divisions (Cockburn & Henderson, 1998; Gassmann & Reepmeyer, 2005; Henderson & Cockburn, 1996). Therefore, divestments of core business are expected to hurt innovations. Should public policy makers be worried about the intuitive risks to innovations that divestment of core business could bring? Not necessarily.

This study argues that the trend in divesting is part of an industry-wide effort to transform large, brand-name pharmaceutical companies from knowledge producers (or inventors of drugs) into knowledge brokers. We argue that brokering knowledge via divestments may help innovations. First, this study examines the trends in divestments and their effect on innovations. Second we develop and empirically test the moderating effect of the knowledge brokering capabilities of these companies on innovations when they divest. Knowledge brokering capabilities represents a multi-dimensional construct that this study will capture by combining three variables: absorptive capabilities, managerial capabilities and divestment capabilities.

Since we view divestments as a reaction to patent expirations, it is imperative for public policy scholars to understand the effects of divestments on innovations. If
divestments hurt innovations, then patent law revisions and/or extensions may benefit consumers. Many stakeholders, including shareholders, patient advocacy groups, and insurance payers have much to gain or lose from the divestment decisions of this industry. Since each generation of marketable drugs funds the next generation of drug candidates, it is imperative to public health to not let innovations dry up. An innovation gap could impose penalties on R&D in the future because future R&D funding depends on prior drug sales (Schmid & Smith, 2002).

1.02 Current Trends: Background

As the world’s largest brand-name pharmaceutical company, Pfizer divested two major therapeutic areas: allergies and respiratory disease in 2011. GlaxoSmithKline too divested early stage development of drug candidates (Daniel, 2011). Trimming to become lean is how large, brand-name pharmaceutical firms will reinvent themselves from knowledge producers into what Gassmann and Reepmeyer coined as “knowledge brokers” (Gassmann & Reepmeyer, 2005). Gassmann and Reepmeyer (2005) predict that the “pharmaceutical company itself [will] actively support external innovation activities by making financial investments into legal entities that serve as a co-operation partner.” The authors envision pharmaceutical companies would fund, organize and manage innovations outside of the firm (Gassmann & Reepmeyer, 2005), a change from previous decades during which pharmaceuticals companies such as Eli Lilly and Merck carved a niche for themselves through in-house research and development of
breakthrough medicines. On public health grounds, public policy has a stake in the success of core business divestments in this industry transformation.

Part of the divestment of core business is the externalization of R&D. Pharmaceutical companies have divested the early, preclinical stages of drug development. One of the ways in which firms are supporting and creating access to external innovation is through venture funds. An example of a legal entity created by a pharmaceutical company, Novartis, to invest in innovations is the Novartis Venture Fund. The Novartis Venture Fund invests in companies that produce pharmaceutical innovations by providing money on an incremental basis. The Novartis Venture Fund reviews the initial business plan and incremental progress for funding decisions. It invests in firms with candidate products at all stages of development, from preclinical to Phase III clinical trials. Other examples are the Novartis Option Fund and the Novartis Korean Option Fund. Both of these funds invest only in firms that are producing pharmaceutical innovations at the early stages. The Novartis Option Fund invests specifically in high-risk areas, an activity that pharmaceutical companies evidently are not willing to undertake. The Novartis Korean Option Fund invests in biotechnology firms at the early stages in South Korea (“Novartis Venture Funds: Our Funds,” 2012). These funds illustrate one of the ways of externalizing R&D.
1.03 Background on divestments

The terminology of divestments has not been uniform, according to the current literature. Scholars have referred to divestments when discussing spin-offs, equity carve-outs, split-ups and unit sell-offs. Spin-offs are essentially divestures because the parent company gives up control of the spun off unit and directs resources elsewhere (Kester, 2009). Kester’s (2009: 8) study on pharmaceutical innovations defined divestments as a “firm’s adjustments and relocation of its resources through spin-offs, equity carve-outs, split-ups or unit sell-off” (Kester, 2009). Moliterno and Wiersema (2007: 1065) examined resource divestment and defined it as the “disposition of an asset from the firm’s resource portfolio, and the associated factor market transfer of that resource to another firm in the industry (Moliterno & Wiersema, 2007). Hoskisson, Johnson and Moesel (1994: 1207-1208) defined divestments as “sales of assets, or sell-offs, management buyouts of divisions, equity carve-outs and spinoffs . . . not financial or capital structure restructuring” (R. E. Hoskisson, Johnson, & Moesel, 1994). This study will use the Moliterno and Wiersema (2007) definition of divestment specified above. These definitions will aid this study in the development of our model.

Research on divestments is usually conducted within the context of examining corporate restructuring and is often treated as what Kester termed a “side effect.” (Kester, 2009) There has not been a study that examined divestments as a business strategy to patent expirations. We argue that this can be pharmaceutical companies’ reaction to the regulatory environment. Studying divestments in the pharmaceutical
industry is critical as divestments of core business such as R&D units can impact innovations because these are the knowledge-producing units within companies. This study will treat developing novel molecular entities for human consumption as the core competence of large, brand-name pharmaceutical firms. Facing a patent cliff, pharmaceutical companies are divesting in order to stay in business. Firms divest due to pressures from multiple stakeholders. Pressures come from shareholders who wish to improve the performance of firms and also from insurance companies, from government payers, from patient advocacy groups who wish to lower the costs of medication, and from regulatory agencies to make safe and effective drugs widely available to the public. Innovation by firms can collectively address at least some of these stakeholder concerns. Divesting core business is a way of decreasing the costs and risks of R&D in this regulatory environment.

Mergers, acquisitions and divestments are likely to represent corporate reactions to patent expirations. Brand-name pharmaceutical companies grew through mergers and acquisitions in an attempt more to avoid the patent cliff than to augment capabilities or scope. A firm falls off the patent cliff when the most profitable patents expire and there are no comparable patents to replace them. The patent cliff invariably reduces profits. Merging with and acquiring firms with viable patents extends cash flow (Kaitin & DiMasi, 2010). Failing to grow organically through in house research and development, the pharmaceutical industry has attempted to grow instead through mergers and acquisitions. In a study of 137 drug companies that existed from 1950-
Munos (2009) concluded that companies differed widely in their ability to produce new drugs. In a before-and-after study, companies that relied heavily on mergers and acquisition did not innovate as much as companies that didn’t use these strategies. Evidence suggests that mergers and acquisition were not effective strategies for innovation. Munos suggests that larger companies that used acquisitions as an innovation strategy may have suffered a decrease in innovations as a result (Munos, 2009). This is likely one of the reasons why divestments are on the increase for firms that previously grew through mergers and acquisitions.

One can argue that the current spate of divestments is simply a result of over-diversified firms that are now selling unrelated units in order to focus on their core competencies. This trend was evident in the 1980s and 1990s (Pettigrew et al., 2006). However, the recent divestments might be different due to their sale of core, related businesses and not only non-core units (Kester, 2009). This study focuses on the trend in the divestment of core business. It is a very important topic mainly because core businesses are those which house the core competencies of the firm. Theoretically and intuitively, it is very risky to sell these businesses. Nevertheless, firms are undertaking such divestment. We examine these trends and their impact on firm innovation in this study.

There are major public policy consequences when large brand-name pharmaceutical firms divest. The most important is the effect of divestments on innovations. Intuitively, divestments of core business hurt innovations. Divestments of
core business increase cash flow in the short run but divert resources away from creating innovations in the long run. Producing a stream of innovations is important because one generation of marketable drugs funds the next generation of drug candidates. Fewer innovations mean a loss for many stakeholders. For instance, shareholders lose value on their investments, patients suffer from untreated diseases, health insurance companies pay for sicker patients, and both employers and governments pay for lost productivity in terms of sick workers. However, the knowledge brokering capabilities of pharmaceutical companies may enable them to increase innovations through divestments.

1.04 The literature on divestments and innovations across industries

We review the literature on divestments and innovations across industries in order to provide a context for divestments within the specific industry of our interest. The literature on the effect of divestments on innovations is scarce. Most of the literature on the effects of divestments on firm performance has focused on financial performance instead of innovations (Brauer, 2006; Lee & Madhavan, 2010). Financial performance is not an ideal proxy for innovative performance because innovations can take over a decade to develop in the drug industry. The few studies of divestments’ effects on innovations have been mixed. Hoskisson and Johnson (1992) show that divestments have a positive effect on R&D spending as a result of more efficient resource allocation (R. O. Hoskisson & Johnson, 1992). Hitt et al. (1996) show that
divestments have a negative effect on R&D spending because they are all too often used to raise cash to repay debt rather than invest in the future (Hitt, Hoskisson, Johnson, & Moesel, 1996). Previous research has thus used R&D spending to measure innovation. Although shown by these studies to be a suitable measure, R&D spending does not guarantee an innovation.

Scholars have examined divestments from both “retrospective” and “prospective” points of view using the resource based theory. According to Kester (2009), most earlier studies have taken a “retrospective” view, a negative view of divestments that portray them as deals to correct initial mistakes. From a “retrospective” point of view, earlier studies questioned whether divestments are the natural result of low firm performance due to either inappropriate acquisitions or over-diversification (Bergh, 1997; R. E. Hoskisson & Hitt, 1994; Kester, 2009; Markides & Singh, 1997). Over-diversification leads to inefficient use of resources. From a prospective point of view scholars have studied whether firms divest in order to focus on their core activities, not necessarily related to poor firm performance. Studies within the past 15 years tend to view divestments more positively than do earlier studies (Capron, Mitchell, & Swaminathan, 2001; Capron, 1999; van Beers C. & Sadowski B.M., 2003). Recent studies frame divestments as proactive decisions to chase new opportunities. These studies see divestments as a natural adaptive strategy in the coevolution between firms and their market environment. Capron, Mitchell and Swaminathan (2001) have taken a dynamic perspective of divestments (Capron et al.,

1.05 The literature on divestments and innovations within the pharmaceutical industry

There is a large literature gap in how divestitures influence innovative productivity within the pharmaceutical/ biotechnology industries. For instance, spin-offs are one type of divestments and the literature on spin-offs within the pharmaceutical industry is scarce. Most studies offer anecdotal evidence published in trade journals. There are a few case studies in academic journals that tend to focus on individual level analysis (Gassmann & Reepmeyer, 2005).

There is a single, quantitative study on the effect of divestitures on innovation within the pharmaceutical industry. The Kester (2009) study, which was published online as a Master’s thesis, found that in the short run, divestments increase R&D intensity as measured by R&D expenditures over sales. Of the 190 firms in the sample, 18.4% divested in 1997 while 24.2% divested in 2007. R&D intensity is one measure of innovative input. There are different effects on innovations depending on whether the divestment is a core activity that is central to the firm’s business. In 1997, only 32.5% of divestments were of core business whereas in 2007, 50.5% were of core business. Kester found that divestment of noncore activities exerts a greater effect on R&D intensity than divestment of core activities (Kester, 2009). This result suggests that
divesting noncore activities liberates scarce resources to be used for core activities. In other words, this suggests that divesting noncore activities enables the firm to concentrate on what it does best. Interestingly, Kester’s results suggest that larger firms exhibit less R&D intensity than small firms, putting into question the economy of scale, since larger firms are supposed to benefit from efficiency at a larger size (Kester, 2009). Studies on whether large pharmaceutical firms have reached diseconomies of scale have yield mixed results (Cockburn & Henderson, 2001; Graves & Langowitz, 1993; Henderson & Cockburn, 1996). Kester’s preliminary result is also a good starting place to probe the competitive advantage of large, brand-name pharmaceutical firms in creating innovations (Kester, 2009). Using the capabilities perspective, we will argue that large, brand-name pharmaceutical companies are losing their competitive advantage in producing innovations.

1.06 Research Proposal

In Kester’s study of 190 pharmaceutical companies, prior to 2003, most of the divestments consisted of noncore activities. After 2003, most of the divestments constituted core activities (Kester, 2009). Firms divest strategically in order to refocus on their core business by shedding divisions that represent what could be considered “over-diversification.” Firms also divest for nonstrategic reason, such as to improve cash flow, reduce debt and restructure their asset portfolios (Markides, 1992). Why then
are large, brand-name pharmaceutical firms increasingly divesting core activities if the purpose of divestments is supposedly to raise cash to fund R&D for core activities?

This study proposes the idea that large brand-name pharmaceutical firms are divesting core businesses in order to shift from being knowledge producers to knowledge brokers. This study tests the effect of divestments on innovations and the moderating effects of large pharmaceutical companies as knowledge brokers. The thesis’s research questions are:

(i) what is the effect of core divestment on innovation and;

(ii) do knowledge brokering capabilities moderate this relationship?

Thus, in this study, we theoretically introduce and empirically explore the construct ‘knowledge brokering’ and examine its role in the relationship between divestment and innovation in the pharmaceuticals industry. This study will use the resource based view, which includes the capabilities perspective. The capabilities theory is suitable for this analysis because drug companies that all have access to similar resources exhibit different capabilities, as evidenced by their heterogeneity in innovative productiveness. We expect divestment of core businesses to be negatively related to innovations but that pharmaceutical companies with high knowledge brokering capabilities would reverse this relationship.
1.07 Public policy implications

The public policy implications of divestments’ effects on innovations are multifaceted and important. If divestments of core business decrease innovations, then divestments will be a detriment to many stakeholders. A decrease in the available medicinal options for patients means a higher burden of disease, fewer years of productivity for workers and fewer quality adjusted life years at the population level (WHO, 2011).

For payers, outpatient pharmaceutical interventions at earlier stages of disease are often more cost effective than inpatient interventions at later stages of disease. For instance, this is the reason why some insurance payers require zero copayments for diabetes drugs for their diabetic policyholders. Pharmaceutical solutions could reduce healthcare costs by preventing exacerbation of disease that requires hospitalizations (American Diabetes Association, 2008; Dall; Henriksson et al., 2000).

The current innovation gap has public policy implications in health economics. Private firms make decisions on which diseases to develop drugs for not based on the burden of disease but on estimates of return on investment. Firm decisions on which disease to research may not perfectly align with public health needs because very difficult disease targets are often higher risk investments. For instance, the high burden of disease for psychological disorders corresponds to less than socially optimum research on psychological disorders and speaks to lack of incentives for firms (Kaitin, 2010). In this scenario, one public policy option is to increase subsidies for in-house R&D
for pharmaceutical companies as a disincentive for divesting out this part of the core business. But this may cause inefficiencies, as there is a diminishing marginal benefit to government subsidies to research. Plus, subsidies shift some of the risk of research from firms onto the government because R&D spending doesn’t guarantee innovations (Karnis, 2010).

On the other hand, if knowledge brokering via divestments increases innovations, then stakeholders will benefit. Furthermore, successful knowledge brokering via divestments can produce a ripple effect in the market if they result in innovations that stimulate investments in pharmaceutical and biotechnology firms. According to Nicholson, Danzon and McCullough (2005), quality signals of a biotechnology firm in the stock market stimulate further investment by venture capitalists and other investors (Nicholson, Danzon, & McCullough, 2005). If knowledge brokering via divestments produce innovations, they may also produce quality signals in the market for both the large pharmaceutical company and the small biotechnology firm. In this scenario, one public policy option is to increase subsidies for biotechnology firms because they will take over some of the knowledge producing roles of brand name pharmaceutical companies. Policy makers should be especially thoughtful about proposing legislation that could create disincentives for biotechnology firms to conduct R&D. For instance, in 2013 the U.S. House passed the Innovation Act (HR 3309), which the biotechnology industry opposed for the bill’s potential to hurt innovations (Association of American Universities. American Council on Education. Association of
1.08 Contribution of this study

Producing innovations within the pharmaceutical industry is a long term consequence because the drug development process is time consuming (Kaitin, 2010). Furthermore, although divestments have been well examined in the literature on corporate restructuring, there is a literature gap on divestments of core businesses within the pharmaceutical industry. Divestments in the short run improve cash flow but in the long run may hamper innovations. Since divestments can produce different consequences in the short term rather than in the long term, this study’s focus on the long term is valuable.

We question whether firms with knowledge brokering capabilities can produce innovations through divestments. In a later section, we will elaborate on the role of knowledge brokers. We introduce the construct of “knowledge brokering” and empirically examine it, which is where we believe our study adds significant value to the existing literature. By doing so, we hope to distinguish between firms which are effective knowledge brokers from those which do not possess these capabilities and their innovations. We focus on divestments, which are an under-studied strategy and also bring out their relevance to the pharmaceuticals industry. Due to our study’s focus
on innovation rather than performance as the dependent variable, our results bear managerial implications and consequences for sustainable competitive advantage.

We argue that divestments are strategic reactions to patent expirations since firm behavior is usually influenced by the regulatory environment. The current spate of divestments potentially marks the transformation of large, brand-name pharmaceutical companies from knowledge producers to knowledge brokers. We discuss this emerging trend within a public policy context. Investment decisions in innovations within this highly regulated industry are naturally sensitive to regulations (Reed, Califf, & Schulman, 2006). If knowledge brokering via divestments increases innovations, we make public policy recommendations for how regulations can help divestments naturally follow.

1.09 A note about the pharmaceutical industry

The pharmaceutical industry is a global industry with tremendous sales and growth potential. Its sheer size and contributions render it a subject worthy of public policy inquiry. In 2012 total global sales reached $962.1 billion (IMS Health, 2013). According to Saftlas (2011), the developed countries included the U.S., Europe (Germany, France, Italy, Spain the U.K) and Japan. The U.S. was by far the largest pharmaceutical market, consuming $310.6 billion. North America consumed 49 percent of all pharmaceutical sales. The emerging markets consumed $150.5 billion with China consuming $41.1 billion and Brazil, India and Russia consuming $48.8 billion (Saftlas, 2011, pp. 14–15). According to the International Federation of Pharmaceutical
Manufacturers and Associations, in per capita terms, pharmaceutical sales also varied greatly across countries. In 2012, the figures ranged from $3 USD in Zimbabwe to $1,077 USD in the U.S. Compared to other geographical locations, consumption per capita was higher in Europe and Japan (International Federation of Pharmaceutical Manufacturers and Associations, 2013).

Brand-name drug companies have spent increased funds on R&D since the mid-1980s. The R&D costs increased in absolute value and as a percentage of sales revenues. The Pharmaceutical Research and Manufacturers of America (PhRMA) estimated R&D costs of its members at $49.4 billion in 2010. On average, brand-name drug companies spent 20 percent of their sales revenues on R&D. The pharmaceutical industry invests more in R&D than do the chemicals, electronics, aerospace and computers industries (Gassmann & Reepmeyer, 2005). Critics of the pharmaceutical industry contend that the patent cliff is caused by insufficient R&D spending at firms. They contend that the current R&D expenditure levels by private firms is social suboptimal (Eichler, 2012). Although this is an important discussion, we point out that this is beyond the scope of this study, which focuses on firm behavior as a reaction to patent expiration. As profit maximizing firms, pharmaceutical companies set R&D expenditures based on their risk tolerance within a given regulatory environment. If studies find that R&D expenditure levels by private firms are indeed suboptimal, then governments need to either reduce the (perception) of risk for firms or create market incentives to increase firms’ risk tolerance.
The high costs of R&D are embedded within the regulatory requirements of safety and efficacy (Kaitin, 2010; “The FDA’s Drug Review Process: Ensuring Drugs Are Safe and Effective,” 2012). The Prescription Drug User Fee Act (PDUFA) of 1992 enabled the U.S. Food and Drug Administration (FDA) to charge drug companies a fee for filing New Drug Applications. From fiscal year 2008-2012 the FDA generated $400 million annually in fees plus $225 million for drug monitoring programs (Saftlas, 2012). The PDUFA set forth three kinds of fees: application, product and establishment. What this means is that a drug company paid an application fee at the time of application submission, an annual fee for products that were previously approved, and an annual establishment fee on approved manufacturing facilities. From 1993 to 2004, the application fee rose from $100,000 to $573,500, a 17 percent annual increase. During these years, the product fee grew from $6,000 to $36,000, also a 17 percent annual increase. During the same time period, the FDA increased establishment fees by 14 percent annually. User fees covered 50 percent of the cost of FDA review on new drug applications. (Berndt, Gottschalk, Philipson, & Strobeck, 2005) The costs of regulations have grown and the costs of doing core business for the pharmaceutical industry have grown. For fiscal year 2014, the FDA raised the new application fee to $2,169,100 for applications with clinical data and 1,084,550 for applications without clinical data. For 2014, the FDA raised the establishment fee to $554,600 and the product fee to $104,060 (The Food and Drug Administration, 2013).
The innovation gap as evidenced by the patent cliff has public policy implications in economics and public health. Patent expirations are followed by the introduction of generics that drive down prices and thereby increase consumer surplus. However, the absence of new patentable drugs hurts consumers with untreated diseases. What drugs or classes of drugs companies chose to develop impacts the burden of disease and the distribution of the burden among countries. According to Kaitin and DiMasi (2010), there is currently a paucity of innovation for drugs that treat diseases with large public health burdens. As Schmid and Smith argued (2002) in the pharmaceutical industry, each new generation of products finances the R&D of the next generation of drug candidates. A failure to innovate imposes penalties against future R&D investments. Both the industry and the public hold an interest in ensuring that the current portfolio of drugs could produce enough innovative products to fund the next generation of drug candidates (Schmid & Smith, 2002, p. 568).

Drug companies face a “patent cliff” as six of the 10 world’s largest selling drugs lost their patents in 2011-2012. The patents of 11 of the top 20 selling drugs in developed countries will expire between 2012 and 2015. From the perspective of the drug companies, a lack of new patentable drugs in the pipelines to replace the expiring patents exacerbates the challenge. For instance, Pfizer’s Lipitor was the world best-selling drug, which lost its U.S. patent protection in 2011. Standard & Poor’s projected the total revenue loss from patent expirations to cost the pharmaceutical industry $120 billion from 2011-2015 (Saftlas, 2012).
Despite the size of the market and blockbuster sales, the industry faces a decline in productivity (Congressional Budget Office, 2006). Brand-name drug makers are under pressure from multiple sides. They face price competition from generic drug makers, price reductions from regulators and payers, increased costs in R&D and decreased R&D productivity. The public reimbursement environment has changed. Most countries with national healthcare systems use a national formulary, which introduces a large degree of uncertainty for pharmaceutical companies. More recently, regulators and payers are increasingly asking drug companies to explicitly prove not only safety and efficacy, but also cost effectiveness, which is a responsibility that was absent in the past and also absent in most other industries. Currently, U.S. government payers are not using cost-effectiveness to determine coverage (IMS Consulting, 2006). In 2013 the U.S. House introduced the Medicare Drug Savings Act (H.R. 1588) to mandate that pharmaceutical companies to provide rebates to low-income consumers (“Medicare Drug Savings Act of 2013 (H.R. 1588),” 2013).

The environment is risky because while facing a patent cliff, brand-name pharmaceutical companies also face a productivity problem. Compared to smaller biotechnology firms, large, brand-name pharmaceutical companies are losing their competitive advantage in producing innovations (Baker & Jasween, 2005; Gassmann & Reepmeyer, 2005). According to a report by global financial services firm Burrill and Company, the pharmaceutical industry may be losing ground to the biotechnology industry in some respects (“Biotech 2013 - Life Sciences,” 2013).
The loss of competitive advantage may be attributed to patent law. Biologics are drugs that are mainly invented by biotechnology firms while small molecule drugs are invented by pharmaceutical companies. The Affordable Care Act of 2010 granted 12 years of patent data exclusivity for biologic drugs, which is seven years longer than the five years granted by the Hatch-Waxman Act for small molecule pharmaceutical drugs. Due to scientific reasons, biologic drugs are also more difficult to imitate or satisfy the FDA bio-equivalency standard for generic companies. The patent law’s longer and stronger protection for patented biologics give biotechnology firms an edge against pharmaceutical companies (Danzan & Keuffel, 2013).

For instance from 2009-2012, the large biotechnology sector grew by 40.6% whereas the large pharmaceutical sector grew by only 17%. During that same time period, the net income in the large biotechnology sector grew by 21.6% whereas net income in the large pharmaceutical sector grew by only 1.1%. From 2009-2012, market capitalization grew by 457% by the large biotechnology sector versus only 17.4% in the large pharmaceutical sector. Most pertinent to this study, R&D spending in the large biotechnology sector grew by 38.7% compared to only 11.7% in the large pharmaceutical sector. As a younger industry, the biotechnology industry has more room for growth than does the more mature pharmaceutical industry (“Biotech 2013 - Life Sciences,” 2013). Despite the biotechnology sector’s smaller base, its increase in R&D expenditure as a percentage of sales is suggestive of the sector’s growing competitive advantage against pharmaceutical companies.
Building on 2009-2012 financial data, the study contends that while smaller biotechnology firms wield a competitive advantage in research capability, large brand-name pharmaceutical companies may wield a competitive advantage in managerial capability. Smaller biotechnology firms may be more innovative, especially in developing biologic drugs but large pharmaceutical companies have the expertise to carry out FDA Phase II and Phase III clinical trials and the sales force to market new drugs. In fact, biotechnology firms in general do not have the capability of carrying out the required FDA clinical trials beyond Phase I (Gassmann & Reepmeyer, 2005; Kaitin, 2010). By divesting the core business of producing innovations, large, brand-name pharmaceutical firms can specialize in shepherding the drug candidates produced by biotechnology firms through the complicated FDA approval process. Thus, large pharmaceutical firms might be strategically divesting to transform themselves from knowledge producers into “knowledge brokers” (Gassmann & Reepmeyer, 2005), a trend which, to the best of our knowledge, has not been empirically explored.

1.10 Firms changed capabilities to seek outside knowledge

The technological environment of drug development has changed drastically due to the recent advancements in molecular biology. The environment outside of the firm holds more valuable knowledge now than it did historically. What the outside environment has to offer to firms has changed because the drug development process has changed, as Henderson and Cockburn contend (1994). The advances in biomedical
science lead drug development away from the traditional use of “random screening” to rational drug design. Random drug screening searched for drug candidates by screening large numbers of compounds and creating libraries of compounds. Traditional random screening, which is no longer the dominant method, gave incentives for each drug company to create large proprietary libraries of compounds because knowledge outside of the firm was not useful. Traditional random drug screening is much less efficient and hence, no longer central to drug research. In contrast, rational drug design used new science to continuously modify a molecule to target specific biochemical pathways. Drug design made it imperative to absorb information from outside the firm, specifically from the scientific, academic communities and public sector (Henderson & Cockburn, 1994, p. 66). Henderson and Clark showed that firms that “systematically revisit the architectural knowledge of the organization” are more likely to outperform their competition (Henderson & Cockburn, 1994, p. 67). By this, the authors meant that competitive advantage comes from reexamining how firms produce knowledge.

According to Powell, Koput and Smith-Doerr (1996) in a study on innovative productivity, large drug companies have the ability to act as “knowledge network” organizers by forming alliances with biotechnology firms. Learning takes place less within firms but rather in “networks of learning.” What the authors meant by this interesting phrase is that large, brand-name pharmaceutical firms can source and connect the knowledge produced by various smaller biotechnology firms and integrate them into the broader scientific knowledge base of a large drug company (Powell,
Koput, & Smith-Doerr, 1996). The importance of knowledge networks to innovating firms within the pharmaceutical and biotechnology industries have been established (Kim & Park, 2010; Kuemmerle, 1997; Wang, 2012; Whittington, Owen-Smith, & Powell, 2009). It is the absorptive capability of pharmaceutical companies that enables them to accomplish this (Cockburn & Henderson, 1998).

Nicholson, Danzon and McCullough (2005) found that such “alliance deals” with large pharmaceutical companies send quality signals to the financial market. The authors’ results indicate that investors increase their valuation of small, unknown biotechnology firms when they announce a deal with a large drug company. These results suggest that investors trust the drug companies’ superior ability to research small, unknown biotechnology firms. This superior ability to research and value biotechnology firms stems from drug companies’ R&D capabilities. Large brand-name pharmaceutical companies’ ability to evaluate and identify valuable research comes from the ability to conduct research. Firms that conduct internal research know now to value the research of other firms (Nicholson et al., 2005). The ability to value biotechnology firms is valuable because it’s tacit and difficult to imitate.

This study argues that knowledge network organizers also make good knowledge brokers. Drug companies use their R&D capabilities to look for new opportunities. In the changing technological environment, drug companies strategically redeploy resources by divesting the core business of knowledge producing to specialize in knowledge brokering.
1.11 FDA Drug Approval Process

The pharmaceutical industry is highly regulated. With the authority of the Federal Food, Drug and Cosmetic Act of 1938, the Food and Drug Administration, hereinafter known as the FDA, regulates new drug approvals in the U.S. The U.S. Department of Health and Human Services (hereinafter known as HHS) is the FDA’s parent organization. In addition to drugs, the FDA also regulates, food, blood products, veterinary products, cosmetics and medical devices (“FDA Basics: What does FDA regulate?,” 2013). The Code of Federal Regulations for Investigational New Drug Applications and New Drug Applications assigns review responsibility to the FDA Centers for Drug Evaluations and Research. The drug development and approval process consists of preclinical and clinical testing. Clinical testing consists of three phases based on a specific enrolled patient population. When a drug company completes preclinical testing in animal models, it submits data to the FDA as part of its Investigational New Drug Application (“How Drugs are Developed and Approved,” 2010).

If the FDA determines that the drug is reasonably safe for human testing and approves the Investigational New Drug Application, the company may move onto Phase I clinical trials for further toxicity testing. Phase I clinical trials usually enroll 20-80 healthy volunteers to test the drug’s side effects, metabolism and excretion (getting rid) of the drug. If the drug doesn’t show unacceptable toxicity (as determined by established FDA rules) in Phase I, the company moves onto Phase II: clinical trials that test for efficacy and short term adverse side effects. Phase II clinical trials usually enroll
12-300 patients with the disease or condition. If the drug shows efficacy, then the company moves onto Phase III clinical trials to establish dosing and drug-drug interactions. Drug-drug interactions are usually adverse side effects produced by drugs interacting with each other instead of with the intended target site in the patient’s body. Phase III clinical trials usually enroll several hundred to 3,000 patients to further test for safety and efficacy. At each subsequent phase of clinical trials, the number of patients enrolled in the study increases because the drug has shown more efficacy and less risk of unacceptable side effects (“The FDA’s Drug Review Process: Ensuring Drugs Are Safe and Effective,” 2012).

In the final step, the drug company submits all testing data, results, labeling information and manufacturing practices as part of the New Drug Application to the FDA. The FDA weighs the drug’s risks and benefits, evaluates the clinical trial’s design, reruns data to replicate results, determines appropriate labeling and inspects the manufacturing facility (which can be domestic or abroad). The drug company pays a user fee to the FDA for its extensive review. In addition, the FDA may require the drug company to commit to post-market studies as a condition of approval (“The FDA’s Drug Review Process: Ensuring Drugs Are Safe and Effective,” 2012). If the FDA approves the drug, the company may market the drug for U.S. sales. If the FDA has not granted its approval of a drug, it may not be marketed for sales in the U.S. but may be sold in other countries (“Guidance: Exports Under the FDA Export Reform and Enhancement Act of
This means that some innovative drugs are available in other countries prior to being available in the U.S. because of the lengthy FDA approval process.

The lengthy and complicated FDA approval process can give large, brand-name pharmaceutical companies a competitive advantage in being knowledge brokers. They are most capable of shepherding the candidate drugs through the FDA approval process. FDA estimated that on average, 13 to 14 of every 20 drugs in Phase I would meet the requirements to successfully pass this phase. Then only nine drugs of the original 20 would pass Phase II. Finally only one or two of the 20 drugs would pass Phase III. Passage of Phase III would not guarantee success, as the FDA may require more testing and information before approval. Finally, only one out of twenty drugs that entered Phase I would receive approval for marketing (Saftlas, 2011). The development process usually requires up to 13 years and only one in 10,000 molecules that are potential drug candidates ultimately come to the market (Gassmann & Reepmeyer, 2005). Clinical trials have increased in size and complexity during the last few decades (Joseph A DiMasi, 2000).

![Drug development process](image)

**Figure 1 Drug development process**
Large, brand-name pharmaceutical companies do not face competition in knowledge brokering from small biotechnology firms or mid-sized pharmaceutical companies because large brand-name pharmaceutical companies are more experienced and efficient in running Phase II and Phase III clinical trials (Gassmann & Reepmeyer, 2005; Kaitin, 2010). Drug discovery, pre-clinical research and Phase I clinical trials are the knowledge producing phases in which biotechnology firms have a competitive advantage. Phase II clinical trials, Phase III clinical trials, submission of a new drug application and post approval study are the knowledge brokering phases in which large, brand-name pharmaceutical companies have a competitive advantage.

By “large, brand-name pharmaceutical companies” this study refers to multinational pharmaceutical firms that produce new molecular entities. Specializing as knowledge brokers, large, brand-name pharmaceutical companies have the opportunity to fulfill a previously unmet need for the services of knowledge brokers. Small biotechnology firms need knowledge brokers who are larger companies to help them shepherd drug candidates through clinical trials (Gassmann & Reepmeyer, 2005). Firms that do not produce innovations may be able to earn high profits if they are able to avoid competition in meeting previously unmet needs of consumers (Roberts, 1999). Due to the high amount of learning and development costs in imitating large, brand-name pharmaceutical companies, there are tremendous barriers to entry in becoming a large, brand-name pharmaceutical company. The barriers to entry such as large R&D costs, renders the role of large, brand-name pharmaceutical firms difficult to imitate.
(Gassmann & Reepmeyer, 2005). There are no firms better postured to become knowledge brokers than large, brand-name pharmaceutical companies.

1.12 Dissertation Format

Chapter One provides a background on divestments’ effects on innovations and presents the dissertation’s thesis along with its contributions. Chapter Two will review the literature of theories on innovations and discuss the variables in detail. Chapter Two will then lay out a conceptual model using the resource based view and the capability perspective. Both these perspectives are useful in explaining divestitures and innovations in research-intensive industries in general and within the pharmaceutical industry in particular. Chapter Three will develop hypotheses on how the independent variables relate to the dependent variables and will address causal inference.

Chapter Four will discuss the methodology of this study, including a description of how the data set was created and how large, pharmaceutical firms were identified for inclusion. Chapter Four also presents the analysis and results. Chapter Five will discuss the results, address the weaknesses of this study and discuss public policy implications of the study results. Chapter Six is devoted to a complementary second part of the study devoted to public policy. We conclude with suggestions for future research questions.
CHAPTER TWO: THEORY DEVELOPMENT

2.01 Resource based view and capabilities perspective

The resource based view has been used extensively to explain heterogeneity among firms in the business strategy literature (Acedo, Barroso, & Galan, 2006; Capron & Mitchell, 1998; Helfat & Peteraf, 2003; Hoopes, Madsen, & Walker, 2003). The resource based view contends that close competitors use their unique combination of resources and capabilities to differentiate themselves from each other and gain a competitive advantage. In order to sustain their competitive advantage, the resources and capabilities need to be valuable, rare and isolated from imitation and substitution (Hoopes et al., 2003). Barney (1991) has defined firm resources as “all assets, capabilities, organizational processes, firm attributes, information, knowledge, etc. controlled by a firm that enable the firm to conceive of and implement strategies that improve its efficiency and effectiveness” (Barney, 1991). This theory assumes that strategic resources are heterogeneous among firms and those resources are not perfectly mobile (Barney, 1991).

Within the conceptual framework of the resource based view is the capabilities perspective. According to Hoope, Madsen and Walker (2003) a capability “is not observable (and hence necessarily intangible), cannot be valued, and changes hands
only as part of its entire unit. A mixture of people and practices continuously enact capabilities . . .” (Hoopes et al., 2003). We will use this definition of the capabilities perspective. The capabilities perspective is useful for this analysis because drug companies that have access to similar resources exhibit different capabilities, as evidenced by their heterogeneity in innovative productiveness (Cockburn & Henderson, 2001; Henderson & Cockburn, 1996, 1994). Cockburn and Henderson use the term resources in a different way than does Barney (1991). Cockburn and Henderson do not include capabilities as resources because they point out that firms with access to similar resources have consistently demonstrated different capabilities. We refer to resources and capabilities separately, as do Cockburn and Henderson.

Morrow et al. (2007) show that valuable and difficult to imitate strategic actions that recombine existing resources make the largest contribution to firm performance during recovery. Strategies need to be valuable and difficult to imitate. Strategies that are not valuable and difficult to imitate do not improve firm performance, as measured by shareholder expectations in the study. Morrow et al. (2007) studied firms suffering from declining performance and used the resource based view to analyze their strategies toward recovery. As a strategy, using the firm’s existing resources to create new products leads to firm recovery (Morrow, Sirmon, Hitt, & Holcomb, 2007). The Morrow et al (2007) study is worthy of discussion because it shows that only strategic actions that are difficult to imitate lead to improved performance. And this study will later discuss why large pharmaceutical companies’ knowledge brokering capabilities are
difficult to imitate. Knowledge based capabilities are not easily transferable or appropriated because these capabilities are difficult to teach and codify. The most valuable knowledge based capabilities are often complex, ambiguous and deeply embedded in the relationships within firms (Nelson & Winter, 1982).

Henderson and Cockburn (1994) found heterogeneity among firms and showed that firm fixed effects explain a large proportion of the variance in research productivity among drug companies, even after controlling for visible factors such as firm size, scope, program size and spillovers (Henderson & Cockburn, 1994). There is, therefore, a theoretical justification for using firm level capabilities to explain strategic behavior and innovative productivity.

2.02 Knowledge Brokering

Hargadon (1998) defines knowledge brokers as “profitably transferring ideas from where they are known to where they represent more innovative possibilities” (Hargadon, 1998). Hargadon gave a useful but overly broad definition. According to a draft report (2012) on knowledge brokering by the U.K.’s National Health Service, knowledge brokers have a “combination of expertise encompassing technology, information management, knowledge selection and development and facilitation” (UK National Health Service, 2013). The National Health Service’s definition is a good general description of the knowledge brokering role that large, brand-name pharmaceutical companies can play. This study will use this definition. This definition is appropriate
because it is broad enough to not be country-specific and it encompasses the capabilities of the multinational firms of our interest.

The U.K. National Health Service has categorized the capabilities of knowledge brokers into three general categories of capabilities. First, knowledge brokers have the capabilities to identify, organize and manage knowledge. Second, knowledge brokers can manage relationships and networks because they are deeply embedded in these networks. Third, they have the capability of “translating knowledge” into practice by disseminating knowledge and monitoring its quality and impact (UK National Health Service, 2013). Some large, brand-name pharmaceutical companies might possess all or some of these general capabilities. We discuss more specific knowledge brokering capabilities that are unique to the drug industry.

2.03 Knowledge brokering capabilities

Based on the capabilities perspective stemming from the resource based view, (Aceno et al., 2006; Cockburn & Henderson, 1998; Kuemmerle, 1997; UK National Health Service, 2013), we can argue that the capability to identify and organize knowledge can be encapsulated in the construct of ‘absorptive capabilities‘. The capabilities required to manage and translate knowledge and relationships can be referred to as ‘managerial capabilities‘. Divestment capabilities are, therefore, also important as pharmaceuticals companies pursue successful knowledge brokering. However, these capabilities are dynamic and not static in nature. We explain this
theoretical development in detail in later sections of our study. Given the dynamic nature of these capabilities, we first give a brief overview of dynamic capabilities in general. Then a discussion of absorptive capabilities, managerial capabilities and divestment capabilities will follow. We explain why these capabilities might play a role in innovation.

2.04 Absorptive capabilities

Not all firms are equally capable of sourcing knowledge from their environment, according to Grimpe and Kaiser (2010) in a study of manufacturing and services firms. Firms with relatively higher internal R&D have more capacity to absorb and exploit external R&D. A firm’s internal R&D, which is a measure of its absorptive capabilities, moderates the relationship between outsourcing R&D and innovative productivity (Grimpe & Kaiser, 2010). The authors found a u-shaped relationship between the level of R&D outsourcing and innovative productivity. Although there are productivity gains from R&D outsourcing, the marginal gains are decreasing/ following a downward slope until firms reach a tipping point, upon which more outsourcing reduces performance. A firm can push the tipping point higher and increase R&D outsourcing and performance if it conducts more internal R&D (Grimpe & Kaiser, 2010). The Grimpe and Kaiser study shows the intricate linkage between research and absorptive capabilities, an idea that is important for the theoretical considerations of this study on divestments.
Cockburn and Henderson defined absorptive capacity as “accumulating the knowledge, skills, and organizational routines necessary to identify and utilize externally generated knowledge (Cockburn & Henderson, 1998). This study will use this definition of absorptive capacity. The ability to absorb knowledge from outside of the firm is especially important for pharmaceutical firms because of the technological change in the drug development process and emerging science (Henderson & Cockburn, 1994).

In another study, Gambardella (1992) also found that firms with superior in-house research are more able to exploit public sector science (government funded research) suggesting that absorptive capabilities play a vital role in innovative productivity (Gambardella, 1992). In turn, multinational entities are also more likely to assign R&D responsibilities to subsidiaries in a country in which the company already had the capacity to absorb new information (Feinberg & Gupta, 2004). These studies contribute to the discussion because we will relate absorptive capabilities to knowledge brokering capabilities. Specifically, this study will argue that absorptive capabilities are a factor component of knowledge brokering capabilities because seeking knowledge from outside of the firm has become crucial to innovating.

Cohen and Levinthal (1989) argued that “while R&D obviously generates innovations, it also develops the firm’s ability to identify, assimilate, and exploit knowledge from the environment – what we call a firm’s learning or absorptive capability” (Cohen & Levinthal, 1989). Cohen and Levinthal emphasized that investing in R&D wasn’t just a short-term investment in learning that paid off when the study
concluded and the findings were in. It was also a long-term investment in the firm’s ability to learn when future knowledge will become available from outside of the firm. Furthermore, in research-intensive industries that also experience knowledge spillovers, developing absorptive capabilities is especially helpful in increasing the return on R&D investments. Making use of competitors’ knowledge spillovers helps the firm stay competitive. Cohen and Levinthal stressed that absorptive capabilities are different from learning-by-doing, which means doing something a little better than before. In contrast, absorptive capabilities enable the firm to do something different from what it has been doing (Cohen & Levinthal, 1989). This study will use absorptive capacity as an independent variable.

2.05 Managerial capabilities

Managerial capability contributes to firm heterogeneity. Holcomb, Holmes and Connelly (2009) found that managers extract value from the resources of the firm. Managers bundle, redeploy and synchronize resources to create value. Managers need to synchronize management processes between bundles in order to gain a competitive advantage. The quality of resources exerts a moderating effect on managerial capability. Managerial capability is more important for firms with lower quality resources than for firms with higher quality resources. Holcomb Holmes and Connelly (200) defined managerial capabilities as tacit abilities developed from experience that is rare and difficult to imitate (Holcomb, Holmes Jr., & Connelly, 2009). An earlier study of
managerial capability’s effect on the firm’s ability to generate rents, Castanias and Helfat (2001) defined managerial capabilities as simply the skills and ability of managers, which is too broad for the purposes of this study (Castanias & Helfat, 2001). This study will instead use the definition of managerial capabilities established by Holcomb, Holmes and Connelly (2009).

Valuable and rare resources are insufficient to gain a competitive advantage in a study by Siromon, Hitt and Ireland (2007). In order to gain a competitive advantage, firms need to effectively manage their resources. Firms create value when they exceed their competitors’ capabilities in producing products that satisfy consumer demand. Within the literature on managerial capability, how firms develop, combine, leverage and re-bundle resources is not well understood (Sirmon, Hitt, & Ireland, 2007).

Haleblain and Finkelstein (1993) found a link between managerial capability and risk. For large firms, the managerial capability and resources of large teams of managers make more impact on firm performance in environments of higher risk than of lower risk. The results of this study stress the importance of managerial capability, especially during times of uncertainty and volatility (Halebian & Finkelstein, 1993). These results are pertinent to this study because the pharmaceutical industry is operating in an environment of higher risk, either due to technological change or by the firms’ choice to pursue higher payoffs. The higher risk can be partially attributed to companies choosing to develop drug candidates with longer development times (Kaitin & DiMasi, 2010; Saftlas, 2012).
Managerial capabilities can be useful in knowledge brokering because knowledge brokers manage information, technology and relationships within networks of learning. The UK National Health Service points out the special function of knowledge brokers in the pharmaceutical industry (2013: 7). “Outside health, knowledge brokers operate in the pharmaceutical industry, where they have a critical role in linking research and development to new product development and then facilitating uptake of new products in healthcare setting” (UK National Health Service, 2013). Large, brand-name pharmaceutical companies bridge the gap between different stages of research, such as the translation of basic research to applied research. Then they disseminate innovations by translating it into practice in clinical sites.

The UK report (2013:14) described the “fundamental importance of a collaborative, networked approach to knowledge brokering, combining strengths from a variety of specialisms and backgrounds” (UK National Health Service, 2013) Large, brand-name pharmaceutical firms have expertise in managing the complicated regulatory responsibilities of conducting Phase II and III clinical trials. Small biotechnology firms do not have the managerial capability to navigate FDA regulations during clinical trials (Gassmann & Reepmeyer, 2005). During Phase II and Phase III clinical trials, large pharmaceutical companies manage relationships with multiple clinical sites and/ or contract research organizations (Baid, 2004). The capabilities of large, brand-name pharmaceutical companies complement the capabilities of small biotechnology firms. This study argues that the difference in capabilities and
specializations will make the knowledge brokering relationship productive. We use managerial capabilities as an independent variable in our model.

2.06 Divestment capabilities

According to Markides (1992), there are many reasons for firms to divest business units. First, firms divest for strategic reasons related to past acquisitions. Firms divest business units that they acquired through acquisition deals that they did not plan to keep from the outset. Firms also divest business units that they had acquired through acquisition deals that they did plan to keep initially but could not successfully manage. In the latter case, firms use divestitures to correct the strategic mistakes made during acquisitions. Second, firms divest in order to refocus on their core business by shedding their over-diversification. Third, firms divest for nonstrategic reasons such as to improve cash flow, reduce debt and restructure their asset portfolios (Markides, 1992).

Firms develop divestment capabilities by divesting and learning from repeated experiences in managing firm disintegration. In a case study of divestitures by an innovative electronics firm, Allen (1998) found that repeated success with spinoffs tend to make firms more likely to use spinoffs in the future (Allen, 1998). Villalonga and McGahan found that firms with divestiture experience are statistically more likely to divest (Villalonga & McGahan, 2005). This result is consistent with previous studies on organizational learning theory and divestment capabilities (plus acquisition capabilities) (Haleblian & Finkelstein, 1993). This study argues that the divestment
experience of large brand-name pharmaceutical companies has helped them develop divestment capabilities. Divestments are complex business processes that require skill to execute well. Divestment capabilities are often ritualized into routines and are thereby, tacit knowledge (Helfat & Peteraf, 2003).

Hitt, Johnson and Moesel (1996) found that firms that had used acquisitions and divestitures prioritized financial controls over strategic controls and thus, were less productive in innovating. Financial controls focus on balance sheets while strategic controls focus on products. Compared to firms that did not use acquisitions and divestitures, firms that did were more likely to seek innovations from outside the firm, a particularly important finding to our study. The authors found that firms that were divesting couldn’t establish strategic controls while they were restructuring. The divestiture process created chaos and imposed high transaction costs. The divestiture disrupted normal operations and thereby diverted managers’ attention away from strategic controls and towards financial controls (Hitt et al., 1996). This study argues that since large pharmaceutical companies are divesting business as a part of their brokering knowledge, these divestitures represent strategic controls rather than financial controls.

Hoskisson and Hitt (1994) didn’t find a relationship between divestiture intensity and internal innovations (R. E. Hoskisson & Hitt, 1994). In a 1992 study, Hoskinsson and Johnson found that when firms used divestitures to refocus, R&D intensity grew overtime. Taken together, these results suggest that the effects of divestitures on
innovations are indirect through control systems (Hitt et al., 1996). Building on Hitt, Johnson and Moesel, this study argues that pharmaceutical companies use their divestment capabilities in knowledge brokering to produce innovations. Compared to firms without divestiture capabilities, firm with divestiture capabilities may be better able to manage the disintegration of slack resources.

In sum, divestment represents the potential preservation of brand-name pharmaceutical companies’ organizational capabilities. Exiting from the innovations producers’ market, brand-name pharmaceutical companies can enter into the knowledge brokers’ market by carving out a niche for themselves. In this case divestment is not the same as dissolution precisely because divestment does not eliminate firm specific capabilities but rather, adapts them to better survive in risky environments.

2.07 Innovations theory

This study adopts the Schumpeterian definition of innovation, which is based on commercialization (Schumpeter, 1947). According to Duane, Ireland and Webb (2007), strategic entrepreneurship is how firms manage the tension between exploiting current competitive advantages and exploring future innovations. There is a tension because what is needed to do both of these well is often antipodal. Efforts to exploit current advantages by standardizing tasks and increasing efficiency may drive out exploration. Exploiting current competitive advantages enables firms to increase efficiency by
centralizing authority and standardizing procedures. Exploring requires some decentralization of authority and relaxation on standardization of procedures. Exploration is how firms anticipate future changes in the environment and take measures to be one step ahead of the game. Exploration makes firms aware of opportunities before their competitors do and thus, may extend the first mover advantage. Operational mechanisms for firms to explore opportunities for competitive advantage include mergers and acquisitions, strategic alliances and corporate venture capital (Duane, Ireland & Webb, 2007). This study argues that exploration has made large, brand-name pharmaceutical companies aware of the market demand for knowledge brokers and their own capabilities of being knowledge brokers.

To Dunlap-Hinkler, Kotabe and Mudambi (2010), exploitative behavior creates incremental innovations while exploratory behavior creates breakthrough innovations. Analyzing over 1,500 new drug approvals by the FDA, the authors found that multinational pharmaceutical firms with a history of producing generic incremental innovations were less likely to produce breakthrough drugs. Firms with a history of producing breakthrough drugs were more likely to produce breakthrough drugs. These results supported the evidence that there was a balance/tradeoff between exploiting and exploring among firms in the business of innovating (Dunlap-Hinkler, Kotabe, & Mudambi, 2010).

In order to enjoy having competitive advantages to exploit in the future, firms need to explore for new scientific knowledge now. Conducting in-house research is one
way to explore. However, firms increasingly acknowledge their own limitations in explorative research. Large brand-name pharmaceutical companies are losing their competitive advantage in producing innovations through internal R&D. Merck published this fact in its 2000 annual report conceding that it contributed to a mere one percent of the global biomedical research (Gassmann & Reepmeyer, 2005). Firms need to successfully absorb information from the environment outside of their own institutions. Knowledge brokering via divestments is a way that large brand-name pharmaceutical companies can simultaneously exploit their managerial capabilities and absorptive capabilities.

Using the resource based view, Roberts (1999) argues that R&D capabilities are what determines pharmaceutical companies’ competitive advantage. Roberts defines innovation within the pharmaceutical industry as new molecular entity that the FDA has approved for marketing. We will use this definition of innovation. Large, brand-name pharmaceutical firms that have R&D capabilities have a demonstrated track record of producing streams of new innovations. R&D capabilities drive innovations, which contributes to competitive advantage. Large, brand-name pharmaceutical firms have earned sustainable profits by producing streams of innovations but their market is contestable and their profitability depends on their ability to produce new streams of innovations (Roberts, 1999).

Facing both a patent cliff and rising expenditures on R&D suggest that brand-name pharmaceutical companies’ R&D capabilities are lagging. The driver of innovations
is R&D in this research-intensive industry. The average cost to bring a drug to market rose from $54 million in 1976 to $1 billion in 2005 (Gassmann & Reepmeyer, 2005, pp. 235–236). Kaitin estimated the average cost to bring a drug to market to be $1.32 billion in 2005 (Kaitin, 2010). Merely 27 percent of companies were able to bring drugs to market at less than $1 billion per drug in 2008. The blockbuster strategy is failing and companies need to develop and market new capabilities in knowledge brokering to yield innovations for the future.

2.08 The impact of regulations on innovations

According to Clement and Harris (2009) innovation can be either incremental or radical. Incremental innovation is less risky to produce by the producer but is also less beneficial to the consumer. Radical innovation is more risky to produce by the producer but also more beneficial to the consumer. Regulations can influence a firm’s decisions to produce incremental versus radical innovation (Stewart, 2010). In a cross-country comparison of regulations, Clement and Harris (2009) found that countries that set higher regulatory standards for drugs had firms that produced more innovative drugs. Higher regulatory standards improved firm capability and competitiveness. Furthermore, higher domestic regulatory standards may also improve firm competitiveness abroad, based on arguments of resource efficiency (Clement & Harris, 2009). Although the reverse causality argument cannot be ruled out, it is less likely that innovative firms strategically locate to countries that set higher standards of
regulations, (such as Japan) since regulations increase the cost of doing business. Large brand-name pharmaceutical companies are multinational entities that make strategic decisions based on each country’s regulatory environment (Stewart, 2010). Regulations on public payer reimbursement (Medicare and Medicaid) do not pay for more innovative drugs at higher rates. Thus, in the U.S. the pharmaceutical industry strategically develops follow-on or “me-too” drugs to extend the life of the patent by creating insignificant innovations, such as differences in dosage and time release (Tironi, 2010). This result suggests that the regulatory environment of the U.S. may not have stimulated pharmaceutical companies to fully develop their R&D capabilities.

On the one hand, regulations stimulate innovations by creating a market for commercialized products, such as medicines in this case. According to Hamburg (2010) prior to FDA regulations, there wasn’t a large market for drugs because of the quality uncertainty. Since consumers couldn’t examine the safety and efficacy of drugs that the producers were advertising, there was information asymmetry between consumers and producers. Producers had more information about the medicines than consumers. Some drugs were lemons and consumers couldn’t distinguish between lemons and valuable drugs. This information asymmetry was too large to support the development of a market. As a result, transactions that would have benefited consumers and producers didn’t take place because of the quality uncertainty. Thus, consumers consumed less than the socially optimum amount of medicines (Hamburg, 2010).
When the FDA began regulating the pharmaceutical industry, it essentially certified the quality of drugs and thereby reduced the information asymmetry between producers and consumers. The FDA helped consumers distinguish between lemons and valuable drugs. This reduction in information asymmetry created a market for pharmaceuticals and thus stimulated innovations. Given the greater amount of drugs that consumers are now willing to purchase when there is more complete information, the FDA regulations created compliance value for the producers (Hamburg, 2010; Stewart, 2010).

On the other hand, regulations may also discourage innovations in several ways. As According to Golec, Hegde and Vernon (2010), regulations create uncertainty in return on investments in innovations. Initially, part of the regulatory burden is policy uncertainty, such as when a regulator applies rules or standards in a confusing manner and firms perceive expectations to be contradictory. Firms have been shown to delay innovating until the policy uncertainty decreases. Second, regulations introduce compliance uncertainty when a firm isn’t sure if it can pass the established regulatory standards, FDA approval to market a drug in this case. Compliance uncertainty also includes the risk that the amount of time needed to pass the established regulatory standards is much longer than a firm anticipated. This risk is particularly high in the pharmaceutical industry, given the lengthy development times of drugs. Third, part of the regulatory burden is price uncertainty. As Golec, Hegde and Vernon (2010) suggest, the mere introduction of the Health Security Act of 1993 for congressional consideration
hurt innovations. The act called for price controls on drugs. The act was never passed but the proposal reduced the number of clinical trials and reduced R&D expenditures by $1 billion in the pharmaceutical and biotechnology industries (Golec, Hegde, & Vernon, 2010). Clearly, pharmaceutical firms are reacting strategically to their regulatory environment.

There have been congressional efforts to streamline the regulatory process to improve the environment for pharmaceutical innovations. A highly regulated industry carries policy risks such as when regulations increase the R&D costs. Three major pieces of legislation have been passed to stimulate innovations: The Bayh-Dole Act of 1980, the Hatch-Waxman Act of 1984 and the Prescription Drug User Fee Act of 1992. According to studies that evaluated the acts, the first two acts produced mixed and uncertain effects on innovations (Kesselheim, 2011; Zerhouni, 2004a, 2004b). The length of patent protection afforded by the Hatch-Waxman Act has been subsequently reduced by the U.S. judicial system (Danzan & Keuffel, 2013). Pharmaceutical companies perceived the reduced patent protection as a serious regulatory risk. The results are summarized in Table 1. The third act reduced FDA review time and expedited the introduction of drugs onto the market (Philipson, Berndt, Gottschalk, & Sun, 2008) but did not eliminate the innovation gap. We discuss the third act in detail.
Table 1 Major legislation

<table>
<thead>
<tr>
<th>Act</th>
<th>Year enacted</th>
<th>Intent</th>
<th>Effect</th>
</tr>
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<tbody>
<tr>
<td>Bayh-Dole Act</td>
<td>1980</td>
<td>Encourage commercial development of intellectual property funded by the Federal government. Granted patent rights to small businesses and nonprofit organizations and licenses to firms.</td>
<td>Mixed. The studies showed that government funded research contributed heavily to drug development. However, the studies did not affirm innovation depended on passage of the Act or licensing process.</td>
</tr>
<tr>
<td>Hatch-Waxman Act</td>
<td>1994</td>
<td>Extended the patent term by the duration of FDA review plus half the time of clinical trials, not to exceed a total of five years.</td>
<td>Uncertain. Although it increased market exclusivity for brand name drugs, studies were not able to link the Act to more innovations.</td>
</tr>
<tr>
<td>Prescription Drug User Fee Act</td>
<td>1992</td>
<td>Enabled the FDA to charge drug companies a fee for filing New Drug Applications. Mandated time limits for completion of review of applications.</td>
<td>Successful. Enabled the FDA to hire more reviewers to increase its workforce by 85% in the decade since Congress enacted the law. The act reduced review time.</td>
</tr>
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2.09 Prescription Drug User Fee Act of 1992

The Prescription Drug User Fee Act (PDUFA) of 1992, which was subsequently renewed, enabled the FDA to charge drug companies a fee for filing New Drug Applications. The regulation’s intent was to decrease compliance burdens while meeting safety and efficacy standards set by the FDA. The fees enabled the FDA to hire more staff to reduce review times. The Act set performance goals for review of new drug applications within specified time periods. The Act established new procedures for holding formal meetings between the FDA and drug companies and procedures to resolve disputes between the agency and drug companies. The meetings with the FDA early during the development process reduced clinical development time (Berndt et al., 2005; Saftlas, 2012).

Philipson et al (2008) conducted a cost-benefit analysis of PDUFA and found that it raised both producer surplus and consumer welfare. Producer surplus represents firm profits. Consumer welfare is raised when novel drugs reach the market earlier due to faster review times, as mandated by the Act. They estimated PDUFA raised producer
surplus (innovative returns) by $7 to $11 billion and consumer welfare by $7 to $20 billion (Philipson et al., 2008). We include a dummy variable to account for the passage of PDUFA to control for the effect of this regulation on innovations.

Yet, despite all of these efforts to streamline the regulatory approval process, most biotechnology firms do not have the capabilities to navigate this process. Only large brand-name pharmaceutical companies have the capabilities to conduct clinical trials beyond the first phase. This unique capability gives large brand-name pharmaceutical companies a competitive advantage to strategically divest core business to transform their core business into knowledge brokering. Part of knowledge brokering is shepherding drug candidates developed by biotechnology firms through clinical trials.

2.10 The innovation gap caused by the decisions of the firm

Although the regulatory environment has increased the costs and risks of innovating for the industry, risk is also attributable to the decisions of the firm. Drug companies are pursuing drug candidates with higher risks because they offer the opportunity for higher reward. Some authors have mentioned that drug companies are pursuing more difficult targets because the low hanging fruit have already been picked in the developed market (Kaitin & DiMasi, 2000). What is also mentioned but not emphasized is the lack of ability by drug companies to identify candidate drugs with blockbuster potential. For instance, Warner-Lambert did not expect Lipitor to sell well and hence, almost canceled its development (Scherer, 2010). It’s the combination of
betting high stakes on developing a blockbuster drug but not knowing which one that
drug might be in the portfolio of projects that increases the risk in firm behavior.

Drug companies are pursuing projects with high failure rates, as measured by
termination of testing in either the preclinical or clinical stages, which increases R&D
costs (Saftlas, 2012). The cost of R&D has grown by 13.4 percent annually since the
1950s. The costs of inputs have risen 49 times faster than the rate of inflation (Munos,
2009). These projects have larger, more complex clinical trials and require expensive,
new technology to drive up R&D costs. Specifically, Gassmann and Reepmeyer
attributed the more complex clinical trials to the need for differentiating new drugs.
They also attributed the increase in R&D costs to funding too many embryonic projects
that did not show early promise or ultimately led to innovation. This supports the
argument that firms lack the ability to identify which candidate drugs among their
portfolios have blockbuster potential (Gassmann & Reepmeyer, 2005). The new
technology such as high throughput screening and combinatorial chemistry drastically
increased the number of potential drug candidates, yet without complementary new
technology to identify the most promising drug candidates for further development,
these new technologies simply increased costs (Kaitin, 2010)

Drug companies terminated drug candidates for scientific and economic reasons
at Phase I clinical trials. Drug companies chose to terminate drug development when the
pharmaceutical market was already crowded, as often the case for chronic drugs to
treat hypertension, arthritis, hypercholesterolemia and depression (Kaitin, 2010). Next
in the development stage, the high failure rate of 52 percent at Phase II clinical trials also makes R&D very costly (Gassmann & Reepmeyer, 2005). On average the FDA approved only 16 percent of all drugs entering clinical trials, ranging from a respectable 27 percent for anti-infectives to merely eight percent for neuropharmacologic drugs and seven percent for cardiovascular drugs. By pursuing more difficult candidate drugs, companies have also had to deal with lower patient enrollment and retention rates (Kaitin, 2010).

The average cost to bring a drug to market rose from $54 million in 1976 to $1 billion in 2005 (Gassmann & Reepmeyer, 2005). Using proprietary data not accessible to many researchers, the Tufts Center for the Study of Drug Development at Tufts University estimated the average cost to bring a drug to market to be $1.32 billion in 2005 (Kaitin, 2010). Merely 27 percent of companies were able to bring drugs to market at less than $1 billion per drug in 2008 (Munos, 2009). Only three out of every 10 drugs that reached the market recouped its R&D costs (Gassmann & Reepmeyer, 2005). Twenty percent of the top selling drugs accounted for 70 percent of the total returns. For instance, Pfizer’s eight blockbuster drugs generated 80 percent of its total sales revenues. Companies chose to pursue high-risk projects because the rewards created the incentive for them to do so. Drug companies have traditionally strategized to produce blockbuster drugs (Gassmann & Reepmeyer, 2005).

The pharmaceutical industry shoulders a high regulatory burden to meet FDA standards but the FDA review time cannot fully account for the innovation gap In the
pharmaceutical industry companies decide to bring a product to market based on technical and scientific ones such as efficacy and safety. The decision hinges on FDA approval (Gassmann & Reepmeyer, 2005). The average time FDA spent on drug review decreased to 1.2 years in 2005-2009 (Kaitin & DiMasi, 2010). The FDA approved 30 drugs in 2011, 11 of which were orphan drugs. Fifty seven percent of the 30 approved drugs in 2011 were reviewed under the FDA accelerated, priority review or fast-track programs (Saftlas, 2012). The percentage of drug applications for priority review was higher in 2000-2009 than in the past 30 years (Kaitin & DiMasi, 2010). The FDA reviewed thirty-four of the 35 drugs it approved within the timeframe of Prescription Drug User Fee Act (Saftlas, 2012). Since the passage of this Act has decreased the approval review times, the FDA review time cannot explain the innovation gap.

Drug development time increased because drug companies chose to pursue targets with longer clinical phases during the 1990s (Kaitin & DiMasi, 2010). The development time spent on preclinical research has remained the same for the past three decades (Gassmann & Reepmeyer, 2005). The clinical phases increased because drug companies increased the number of classes of drugs that intrinsically required longer development times, such as central nervous system and antineoplastic drugs. From 1980-1989 the FDA approved only 20 central nervous system drugs. In contrast, from 2000-2009 the FDA approved 27 central nervous system drugs. From 1980-1989 the FDA approved only 11 antineoplastic drugs. In contrast, from 2000-2009 the FDA approved 47 antineoplastic drugs. On average, central nervous system drugs required
8.1 years to develop and antineoplastic drugs required 6.9 years to develop. Drug companies also decreased the proportion of drugs in their development portfolio that required shorter development time, such as AIDS antiviral drugs that on average required only 4.6 years to test in the clinical phase (Kaitin & DiMasi, 2010).

Central nervous system drugs took 76 percent longer to develop than did AIDS antiviral drugs. Anti-infective drugs took only 5.4 years to develop and drug companies decreased development of them from 51 in the 1980s to 30 in the 2000s. Yet, drug companies chose not to pursue antiinfective drugs because the financial incentives were low. The longer clinical phases of the drugs in development offset the shorter amount of time the FDA took to review applications (Kaitin & DiMasi, 2010). FDA approvals dropped from 53 in 1996 to only 35 in 2011 (Gassmann & Reepmeyer, 2005; “Press Announcements--FDA: 35 innovative new drugs approved in fiscal year 2011,” 2011)

2.11 Theoretical model

We employ a definition of knowledge brokering here which is theoretically solid as well as practically applicable. According to a draft report (2012) on knowledge brokering by the U.K.’s National Health Service, knowledge brokers have a “combination of expertise encompassing technology, information management, knowledge selection and development and facilitation” (UK National Health Service, 2013). The National Health Service’s definition is a good general description of the knowledge brokering role that large, brand-name pharmaceutical companies can play. According to the U.K.
National Health Service, knowledge brokers have the capability to identify, organize, manage and translate knowledge, and to manage relationships (UK National Health Service, 2013). Based on the capabilities perspective stemming from the resource based view, (Acedo et al., 2006; Cockburn & Henderson, 1998; Kuemmerle, 1997; UK National Health Service, 2013), first, we can argue that the capability to identify and organize knowledge can be encapsulated in the construct of ‘absorptive capabilities’. Second, the capabilities to manage and translate knowledge and relationships can be referred to as ‘managerial capabilities’. Third, divestment capabilities enable pharmaceuticals companies to pursue successful knowledge brokering.

We expect divestment of core businesses and innovations to be negatively related but we also expect knowledge brokering capabilities to reverse this relationship. Knowledge brokering capabilities is a multi-dimensional construct that this study will capture by combining three variables: absorptive capabilities, managerial capabilities and divestment capabilities. The ability to extract information from outside of the firm, identify new market opportunities and redeploy resources to manage information are crucial capabilities in knowledge brokering. The theoretical justifications for the use of these three variables are supported by the literature. These three capabilities can be understood as factors to represent knowledge brokering capabilities.
Figure 2: Theoretical model of the effect of core divestments
Figure 3 Theoretical model of the effect of divestments moderated by knowledge brokering
CHAPTER THREE: HYPOTHESIS DEVELOPMENT

We devote this chapter to developing our hypotheses. The dependent variable is innovations and the independent variables are divestments and knowledge brokering capabilities. There are three factors in knowledge brokering capabilities: absorptive capabilities, managerial capabilities and divestment capabilities. We will discuss our expectations of how each of these three factors will moderate the relationship between divestment of core businesses and innovations.

3.01 Divestment of core businesses and innovations

The divestment of core businesses is a very important topic mainly because core businesses are those that house the core competences of the firm. Core businesses strategically differentiate firms from their competitors in the market. Leonard-Barton defined a core capability as an “interrelated-interdependent knowledge system (Leonard-Barton, 1992, p. 114)” Also called firm specific competences, core competences are what the business could commercialize and market (Leonard-Barton, 1992, p. 114; “Novartis: Acquisitions and divestments,” 1999). Theoretically, it is very risky to sell these businesses. Nevertheless, firms are undertaking such divestment.

Lei, Hitt and Bettis (1996) defined core competence as “a central set of problem-defining and problem solving insights that enable the firm to create potentially
idiosyncratic strategic growth alternatives and to enact, at least partially, its environment” (Lei, Hitt, & Bettis, 1996). This study will treat developing novel molecular entities for human consumption as the core competence of large, brand-name pharmaceutical firms. The competence to develop novel molecular entities for human consumption differentiates brand-name pharmaceutical companies from other firms in other industries.

Large, brand-name pharmaceutical firms’ core business differentiates them because non-pharmaceutical firms do not have the competence to develop novel drugs for human consumption as a non-core business. Examples of none core businesses for brand-name pharmaceutical companies include over-the-counter drugs, animal medications, agri-business, nutritional supplements, consumer personal care products, medical devices and diagnostics (“GlaxoSmithKline provides further update on divestment of non-core over-the-counter (OTC) brands,” 2012; Silverman, 2011).

We expect a negative relationship between the divestment of core businesses and innovations. Divestment of core businesses means selling core capabilities that are embodied in the business. Core capabilities for pharmaceutical companies have historically been R&D and they are valuable because they are what determined a firm’s competitive advantage. Selling core capabilities means selling what the firm does best. Selling core businesses is relinquishing that which differentiates the firm from competitors in the market and potentially reducing the firm’s competitive advantage (Leonard-Barton, 1992). For large, brand-name pharmaceutical companies, selling R&D
units constitutes selling core businesses because research is the engine of innovations (Cockburn & Henderson, 1998; Henderson & Cockburn, 1994; Kester, 2009). Historically, large, brand-name pharmaceutical companies have earned a dominant market position and sustained profits by innovating. Their sustained profits depended on a stream of new blockbuster drugs from which they demonstrated with a track record of R&D capability (Roberts, 1999). With fewer core businesses, brand-name pharmaceutical companies are left with less of what they do best. In the short run, selling these assets improves the balance sheet but in the long run, selling them for nonstrategic reasons may hamper innovations.

_Hypothesis 1: Divestment of core business is negatively related to innovations._

According to a draft report (2012) on knowledge brokering by the U.K.’s National Health Service, knowledge brokers have a “combination of expertise encompassing technology, information management, knowledge selection and development and facilitation” (UK National Health Service, 2013). We use the UK definition of knowledge brokering because it is a practical definition that is particularly useful for our model. Building upon this definition, we argue that for large brand-name pharmaceutical companies, knowledge brokering means integrating outside knowledge into learning networks, managing relationships along the value chain and using these relationships to transfer profitable knowledge to commercialization. Using these three capabilities to
broker knowledge via divestments is likely a strategy used by large, brand-name pharmaceutical firms to maintain organizational capability and develop new competitive advantages.

3.02 Absorptive capabilities

We argue that through divestment of core businesses, large, brand-name pharmaceutical companies sell knowledge producing units to buyers who can increase the value of these assets by producing drug candidates. Pharmaceutical firms’ absorptive capabilities enable them to identify knowledge outside of the firm and integrate pieces of new knowledge into a larger scientific landscape. Pharmaceutical companies know how to assess the research portfolios of biotechnology firms. Pharmaceutical companies have superior ability to research biotechnology firms (Nicholson et al., 2005) and thereby, identify the suitable buyers. A promising drug candidate created by a biotechnology firm may further be developed and tested by a large pharmaceutical company. This ability to identify particularly suitable buyers may change the relationship between divestment of core business and innovations. Intuitively, we expect divestment of core business to be negatively related to innovations. But moderated by pharmaceutical firms’ absorptive capabilities, we expect this relationship to be positive.
3.03 Managerial capabilities

Managerial capabilities enable large, brand-name pharmaceutical companies to innovate by shepherding promising drug candidates through Phase II and Phase III of FDA clinical trials. The biotechnology industry is a young industry. Castanias and Helfat found that industry specific managerial capabilities tend to be rare in young industries (Castanias & Helfat, 2001). This study argues that because of the youth of the industry, smaller biotechnology firms do not have the managerial capability to navigate complicated FDA regulations. Hence, large, brand-name pharmaceutical companies can adopt running clinical trials as their core business with limited competition (Gassmann & Reepmeyer, 2005). With their managerial capabilities giving them a competitive advantage in running clinical trials, large, brand-name pharmaceutical companies have positioned themselves to become knowledge brokers.

Kaplan, Murray and Henderson (2003) found that strategic business decisions in response to technological change in biotechnology were dependent upon senior managers identifying and recognizing the change. Technological change offers a risk and an opportunity. As measured by patents and publications, successful in-house research is not the engine that drives managers to identify the technological change. This result suggests that managerial capability can contribute to business strategies independent of in-house research capabilities (Kaplan, 2003).

Large brand-name pharmaceutical companies are in the process of strategically changing their core business from producing new molecules to managing the regulatory
requirements of developing new molecules produced by entities outside of the firm. In turn, we argue that the relationship between divestment of core business and innovations is moderated by managerial capabilities. Specifically, among companies with a high level of managerial capabilities, there may be a positive relationship between divestment of core businesses and innovations.

3.04 Divestment capabilities

Divestments represent the potential preservation of brand-name pharmaceutical companies’ organizational capabilities. Firms develop divestment capabilities by divesting and learning from repeated experiences in managing firm disintegration. Allen (1998) found that repeated success with spinoffs tend to make firms more likely to use spinoffs in the future (Allen, 1998). Villalonga and McGahan found that firms with divestiture experience are statistically more likely to divest (Villalonga & McGahan, 2005). We argue that the divestment capabilities of large, brand-name pharmaceutical firms may help them to divest and innovate via knowledge brokering.

Firms differ in their abilities to handle firm disintegration. The divestiture process creates chaos and imposes high transaction costs. Divestitures disrupt normal operations and thereby diverted managers’ attention away from strategic controls (Hitt et al., 1996). We argue that among large brand-name pharmaceutical companies adept at handling firm disintegration because they have experience divesting, these
transactions may overcome their transaction costs and thereby, systematically transfer knowledge.

Since the blockbuster strategy of drug development is failing for brand-name pharmaceutical companies, divestment of certain core business units may also liberate resources to devote to knowledge brokering. Divestments may enable brand-name pharmaceutical companies to manage more relationships in learning networks and scale up shepherding drug candidates through FDA regulatory requirements.

Teece argues that firms that innovate need to establish relationships, vertically and horizontally for the sake of forming complementary assets in order to compete (Teece, 1992). The divestment of core businesses may be the process of complementary asset formation between knowledge producers who are biotechnology firms with knowledge brokers who are large, brand-name pharmaceutical companies. We expect a positive relationship between divestment of core business and innovations among large, brand-name pharmaceutical companies with divestment capabilities.

_Hypothesis 2a: Divestment of core business is negatively related to innovations for firms with lower levels of knowledge brokering capabilities, absorptive capabilities, managerial capabilities and divestment capabilities._
Hypothesis 2b: Divestment of core business is positively related to innovations for firms with high levels of knowledge brokering capabilities, absorptive capabilities, managerial capabilities and divestment capabilities.
CHAPTER FOUR: METHODOLOGY AND RESULTS

4.01 Regression Analysis – 2 Stage Least Squares (SLS)

Regression analysis is an established methodology in studies of pharmaceutical innovations (Joseph A DiMasi, 2000; Kaul, 2012b; Kester, 2009; Kutyavina, 2010). This study uses 2-stage least squares regression analysis. Preliminary analysis using ordinary least squares (OLS) analysis suggested endogeniety, as evidenced by the Hausman Test for endogeniety (p = 0.0737). Theoretically, we have reason to believe that innovations would influence divestment capability, as measured by betweenness centrality values derived from divestment network analysis. The problem is that betweenness centrality correlated with the disturbance term of the OLS equation. To address the endogeniety problem, Gujarati and Porter recommend creating an instrumental variable to run 2-stage least squares analysis. The instrumental variable should proxy the endogenous explanatory variable but be uncorrelated with the disturbance term (Gujarati & Porter, 2008). Thus, we have created a variable on mergers and acquisitions capability (called “instrument”) as an instrumental variable to proxy the betweenness centrality variable derived from divestment network analysis. Betweenness centrality and the instrumental variable have a 0.185 correlation, which suggests that it is appropriate as a proxy and instrumental variable.
The unit of analysis is at the firm level. Many firms are subsidiaries of other firms. Hence, we derive each target unit’s parent firm using the ultimate parent primary ticker symbol listed in our database. Then we identify the name of the ultimate parent by searching for the ticker symbol in Morningstar, Bloomberg and Yahoo Finance (Morningstar, 2014; Bloomberg 2014, Yahoo, 2014). Data points for which ticker symbols could not be successfully searched were dropped.

To define inclusion and exclusion criteria, we extracted divestment data for deals with effective dates of 1994-2003. We included data points with divestitures that were affirmed and deal statuses listed as complete. We excluded data points with acquirers listed as “investors”, “investor group” or undisclosed and missing or ultimate parent primary ticker symbols listed as unknown. We use STATA software version 11.2 for statistical analysis and Gelphi software version 8.2 for network analysis.

4.02 Dependent variable: clinical trials

Although past studies of innovations within the pharmaceutical industry have used citation-weighted patents and found them to be useful proxies (Hall, Jaffe, & Trajtenberg, 2005; Henderson & Cockburn, 1994; Mazzucato, Tanconi, & Dept, 2006; Qian, 2007), patents are not ideal measures of pharmaceutical innovations. Patents represent very early discoveries that may not come to fruition in the market. Since our definition of innovations is pegged to marketability and pharmaceutical innovations require regulatory approval, measures of innovations at later stages of drug
development would be more appropriate (Wang, 2012). For these reasons, we use clinical trials to measure innovations. We obtain clinical trials data from the ClinicalTrials.gov database maintained by the U.S. National Institute of Health. The database includes publically and privately sponsored trials of human subjects worldwide ("ClinicalTrials.gov," 2014).

There are three phases of FDA clinical trials, at the end of which the pharmaceutical company may submit an application for approval to market a new drug. Phase three is closer to marketability than is phase two and phase two is closer to marketability than is phase one. Only drug candidates that pass phase three may qualify for submission of a new drug application to the FDA. This study creates a weight for each phase of clinical trials in order to take the proximity to marketability into account. DiMasi, Feldman and Scckler calculated the pass rate of drug candidates for each phase to the next phase. Seventy one percent of all drug candidates pass from phase one to phase two. Forty five percent of drug candidates pass from phase two to phase three. And sixty four percent of all drug candidates pass from phase three to the new drug application stage (DiMasi, Feldman, Seckler, & Wilson, 2010). For each firm, we multiple our count of phase one by 0.71 x 0.45 x 0.64. We multiply our count of phase two by 0.45 x 0.64. We multiply our count of phase three by 0.64. Multiplying each clinical trials count by the average pass rate to marketability for its phase means assigning more weight to trials at later stages. The value of our weighted clinical trials variable is the summation of these three products. This method helps us to weigh innovations in each
trial in terms of its closeness to marketability. We collected clinical trials data from January 1, 2007 through December 31, 2013.

4.03 Independent variable: divestments

Villalonga and McGahan (2005) defined divestiture in terms of control, interest and assets (2005:1191) according to the Thomson Reuters SDC database. “A divestiture is tracked in SDC when there is a loss of majority control, the parent company is losing a majority interest in the target, or the target company is disposing of assets. A spin-off is the tax-free distribution of shares by a company of a unit, subsidiary, division, or another company’s stock, or any portion thereof, to its shareholders. SDC tracks spin-offs of any percentage. In contrast, in a carve-out, the new company’s shares are distributed or sold to the public via an IPO. Carve-outs are tracked in SDC only if they represent 100 percent of the unit, subsidiary division or other company” (Villalonga & McGahan, 2005). The benefit of this definition is its specificity. Divestiture data was obtained from the Thomson Reuters SDC Platinum database.

The core business of large brand-name pharmaceutical companies is researching and developing innovative drugs for human consumption. The core business of large brand-name pharmaceutical companies is important because they house the companies’ core capabilities. For this research-intensive industry, R&D is its core business because R&D is the engine that has traditionally driven innovations (Kester, 2009). We argue that any divestment of core business could be expected to negatively
impact innovations. This study uses counts of core divestment as an independent variable to explain innovations. It takes on average 13 years to develop a drug from phase one to phase three of FDA clinical trials (Gassmann & Reepmeyer, 2005). Since we collect data on our dependent variable starting in 2007, we lag our independent variable by 13 years to include divestments made effective from 1994-2003 in the SDC Platinum database.

Previous studies have used SIC codes to differentiate core versus noncore business. Hill and Hansen used SIC codes to differentiate different industries and to identify firm diversification. In their study, SIC codes that are the same showed undiversified firms while SIC codes that are different showed diversified firms (Hill & Hansen, 1991). However, when we manually inspect our data, many obviously noncore divestments that are of animal drug units or personal care units carry core SIC codes 2834, 2836 and 8731. To increase the accuracy of determining core versus noncore divestments, we have done research on each divested unit online and examine the name of each divestment, which sometimes contain giveaway words such as “animal health,” “pet product” or “personal care” in the deal. We expect a negative relationship between core divestments and innovations.

4.04 Independent variable: absorptive capabilities
Henderson and Cockburn (1994) found large heterogeneity among firms and showed that firm fixed effects explain a large proportion of the variance in research productivity among drug companies, even after controlling for visible factors such as firm size, scope, program size and spillovers (Henderson & Cockburn, 1994). There is thus a theoretical justification for using firm level capabilities to explain strategic behavior and innovative productivity. Within the same environment, some firms are better able to absorb and exploit information from outside of the firm. For research intensive firms, this absorptive capability is developed by conducting internal R&D. Experience in research tends to build overtime (Cockburn & Henderson, 1998; Grimpe & Kaiser, 2010) This supports using R&D over sales as independent variables in this study.

This study uses R&D intensity as measured by R&D expenditures over sales as a proxy measure of absorptive capacity. Scholars have struggled to fully capture the multi-dimensional construct of absorptive capability in their measurements. The use of R&D expenditures is methodologically problematic because firms allocate budgets for research based on sales, which are dependent on research success. Although this single dimensional measure is not ideal to represent a multi-dimensional construct, it is an established method used by scholars (Flatten, Engelen, Zahra, & Brettel, 2011). We use a three-year average of R&D expenditure over sales for each firm. Data was obtained from LexisNexis Worldscope Reports. We expect a positive relationship between absorptive capabilities and innovations.
4.05 Independent variable: managerial capabilities

The importance of managerial capability, especially during times of uncertainty and volatility was supported by Halebian and Finkelstein (Haleblian & Finkelstein, 1993). Managerial capability partially takes into account the experience of the firm since learning by managers is adaptive (Eggers, 2012) Fortune and Mitchell (2012) found that managerial capability played an important role in the adaptive strategies of firms in industries that are evolving (Fortune & Mitchell, 2012). This finding is pertinent to our study because we argue that the pharmaceutical industry is evolving. Persaud (2012) studied how the managerial capabilities of firms through surveys of chief executives’ created synergies within the firm (Persaud, 2005). We use the tenure of chief executive officers at each firm as compared to the industry average as a proxy for managerial capability. We assign a code of one to firms managed by chief executives with longer than industry average tenures and a code of zero to firms managed by executives with less than industry average tenures. No firms were managed by chief executives with exactly the average industry tenure. We obtain data from Mergent Online. We also measure managerial capability by the average number of years the executive managers have worked in the pharmaceutical industry. Data is obtained from Mergent Online. When data was not available in Mergent Online, data was manually obtained from the firm’s websites and the manager’s publically available CVs for the four top managers for which the information was available (Mergent Online, 2014). We expect a positive relationship between managerial capabilities and innovations.
4.06 Independent variable: divestment capabilities

Divestment may strategically liberate firm resources for redeployment to other useful activities. For instance, the divestment of a research unit that searches for preclinical drug candidates may liberate resources to enable the firm to conduct more clinical trials. We argue that strategic core divestments may create innovations when the divestment is done by a firm with knowledge brokering capabilities. Thus we derive our divestment capabilities variable (betweenness centrality) from network analysis. Previous studies of this industry have also used betweenness centrality as an explanatory variable for innovations (Wang, 2012). Betweenness centrality is defined as the number of times a firm is in the geodesic path between two other firms. Mathematically it is defined as \( C_B(i) = \sum_{j<k} \frac{g_{jk}(i)}{g_{jk}} \). The term \( g_{jk}(i) \) represents the number of these geodesics that pass through node \( i \) and the term \( g_{jk} \) represents the number of geodesics linking firms \( j \) and \( k \). Betweenness centrality is based on the premise that firms that can go between other firms in transactions have power (Hanneman & Riddle, 2014). We expect a positive relationship between divestment capabilities and innovations.

We also include hub weight as the second part of our divestment capability measure. Hubs are entities that point to good authorities. The relationship is asymmetric in that hubs direct information flow to authorities but may have only a few
links themselves. Kleinberg describes a hub weight as “proportional to the sum of the authority weights of pages that it links to” (Kleinberg, 1999). In this study, authorities are buyers of many divested business units. The calculation for hub weight is as follows.

\[ x(v) = \sum_{(u,v) \in L} w(u, v) y(u) \quad \text{and} \quad \sum_{(v,u) \in L} w(v, u) y(u) \]

\( x(v) \) is the authority weight of vertex \( v \) and \( y(v) \) is its hub weight (Batagelj, 2003). Higher hub weights suggest that a firm is good at directing divestment deals to authorities. We expected a positive relationship between hub weights and innovations.

4.07 Control variable: return on equity

A common firm level control variable for financial performance and risk is return on equity. This variable controls for risk adjusted profitability (Barth, Beaver, & Landsman, 1998; Wang, 2012). Worldscope Reports by Lexis Nexis defines return on equity as the net income divided by the previous year’s common equity in stocks trading on the NYSE, ASE and NASDAQ. The database also provides the five-year average return on equity, which we use to smooth the effects of any given year. Worldscope Reports defines the five-year average return on equity as the arithmetic average of the previous five years. When the five-year average is not available, we use the three-year average, defined as the arithmetic average of the previous three years (“Worldscope database datatype definitions guide,” 2007).
4.08 Control variable: biologics

The Affordable Care Act of 2010 granted 12 years of patent data exclusivity for biologic drugs, which is seven years longer than the five years granted by the Hatch-Waxman Act for small molecule pharmaceutical drugs. Due to scientific reasons, biologic drugs are also more difficult to imitate or satisfy the FDA bio-equivalency standard for generic companies. The patent law’s longer and stronger protection for patented biologics give biotechnology firms a competitive advantage against pharmaceutical companies (Danzan & Keuffel, 2013). Large pharmaceutical companies are thus branching into the business of developing biologics. We count the number of biologic drugs that are in clinical trials for each firm between 2007-2013. Having many biologic drugs in clinical trials is especially suggestive of a pharmaceutical firm’s strategic, adaptive capabilities at overcoming both policy and scientific challenges. Thus we expect a positive relationship between the number of biologic drugs and innovations.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Observations</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squared root of weighted clinical trials</td>
<td>81</td>
<td>2.4045</td>
<td>5.0123</td>
<td>0</td>
<td>21.3432</td>
</tr>
<tr>
<td>Squared root of core divestments</td>
<td>81</td>
<td>1.2169</td>
<td>0.9016</td>
<td>0</td>
<td>4.4721</td>
</tr>
<tr>
<td>Squared root of core x biological drugs</td>
<td>60</td>
<td>2.9809</td>
<td>7.4068</td>
<td>0</td>
<td>37.4166</td>
</tr>
<tr>
<td>Squared root of betweenness centrality</td>
<td>81</td>
<td>0.0387</td>
<td>0.07645</td>
<td>0</td>
<td>0.3331</td>
</tr>
<tr>
<td>Hub</td>
<td>81</td>
<td>0.0099</td>
<td>0.0024</td>
<td>0</td>
<td>0.0196</td>
</tr>
<tr>
<td>CEO tenure</td>
<td>59</td>
<td>14.9164</td>
<td>8.4928</td>
<td>1</td>
<td>38.75</td>
</tr>
<tr>
<td>CEO</td>
<td>63</td>
<td>0.6667</td>
<td>0.4752</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Log of R&amp;D over sales</td>
<td>54</td>
<td>3.0144</td>
<td>1.6405</td>
<td>-1.0498</td>
<td>8.454</td>
</tr>
<tr>
<td>Return on equity</td>
<td>63</td>
<td>-14.0414</td>
<td>99.084</td>
<td>-567.51</td>
<td>136.84</td>
</tr>
<tr>
<td>Squared root of instrumental variable</td>
<td>81</td>
<td>0.6035</td>
<td>0.9969</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>
The highest number of observations is 81 for weighted clinical trials, core divestments, betweenness centrality, hub and our instrumental variable. And the lowest number of variables is 54 for R&D over sales. We also generate correlation coefficients between the variables.

### Table 3 Correlations

<table>
<thead>
<tr>
<th></th>
<th>Clinical weighted trials</th>
<th>Core divestments</th>
<th>CEO</th>
<th>CEO tenure</th>
<th>R &amp; D over sales</th>
<th>Betweenness centrality</th>
<th>Hub</th>
<th>Biological drugs</th>
<th>Return on equity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical weighted trials</td>
<td>1.0000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Core divestments</td>
<td>0.6736</td>
<td>1.0000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEO</td>
<td>0.2162</td>
<td>0.1819</td>
<td>1.0000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEO tenure</td>
<td>-0.0786</td>
<td>-0.1218</td>
<td>0.5694</td>
<td>1.0000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R &amp; D over sales</td>
<td>-0.1259</td>
<td>-0.1251</td>
<td>0.0683</td>
<td>0.0843</td>
<td>1.0000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betweenness centrality</td>
<td>0.3947</td>
<td>0.8403</td>
<td>0.2257</td>
<td>0.0083</td>
<td>-0.0984</td>
<td>1.0000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hub</td>
<td>0.0849</td>
<td>-0.0126</td>
<td>0.1639</td>
<td>0.3495</td>
<td>-0.0370</td>
<td>-0.0668</td>
<td>1.0000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological drugs</td>
<td>0.5978</td>
<td>0.4068</td>
<td>0.2369</td>
<td>-0.1075</td>
<td>-0.1083</td>
<td>0.1422</td>
<td>-0.2597</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>Return on equity</td>
<td>0.2488</td>
<td>0.2975</td>
<td>0.3018</td>
<td>0.3018</td>
<td>0.1616</td>
<td>0.2683</td>
<td>0.0424</td>
<td>0.1179</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

There is a high correlation of 0.8403 between core divestments and betweenness centrality. There is also a high correlation of 0.6736 between core divestments and weighted clinical trials. There is a moderately high correlation of 0.5978 between clinical trials and the biologics count, suggesting that firms with the capability to develop biologic drugs may be more capable of innovating.

To linearize the relationship between dependent and independent variables, we generate distributional tests and plots in STATA. These tests indicate a need to transform the variables. The distributions for clinical trial weights, core divestment counts, betweenness centrality and firm size exhibit moderate skew. Tests suggest that
clinical trial weights, core divestment counts and betweenness centrality should be transformed by taking the square roots of their values. R&D over sales exhibits skew. Tests suggest that R&D over sales should be logged. We keep managerial capability, hub weights and return on equity untransformed, as suggested by the tests.

Table 4 Regression results and post estimation tests

<table>
<thead>
<tr>
<th>2 Stage least squares</th>
<th>Number of obs = 29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (centered) SS = 1285.3272</td>
<td></td>
</tr>
<tr>
<td>Total (uncentered) SS = 2322.3212</td>
<td></td>
</tr>
<tr>
<td>Residual SS = 471.1931</td>
<td></td>
</tr>
<tr>
<td>F(8, 20) = 4.78</td>
<td></td>
</tr>
<tr>
<td>Prob &gt; F = 0.0021</td>
<td></td>
</tr>
<tr>
<td>Centered R-squared = 0.6334</td>
<td></td>
</tr>
<tr>
<td>Uncentered R-squared = 0.7971</td>
<td></td>
</tr>
<tr>
<td>Root MSE = 4.031</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical weighted trials</th>
<th>Coefficients</th>
<th>Standard error</th>
<th>z</th>
<th>P &gt;</th>
<th>[95% Confidence Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core divestments</td>
<td>47.5659</td>
<td>21.4704</td>
<td>-2.2200</td>
<td>0.027</td>
<td>5.484694 - 89.64701</td>
</tr>
<tr>
<td>CEO</td>
<td>-3.3909</td>
<td>2.0700</td>
<td>-1.6400</td>
<td>0.101</td>
<td>-7.448091 - 0.6663185</td>
</tr>
<tr>
<td>CEO tenure</td>
<td>0.5719</td>
<td>0.1173</td>
<td>4.8700</td>
<td>0.000</td>
<td>0.3419278 - 0.8017889</td>
</tr>
<tr>
<td>R &amp; D over sales</td>
<td>617.2209</td>
<td>269.1977</td>
<td>2.2900</td>
<td>0.022</td>
<td>89.60308 - 1144.839</td>
</tr>
<tr>
<td>Betweenness centrality</td>
<td>-0.1854</td>
<td>0.1447</td>
<td>-1.2800</td>
<td>0.200</td>
<td>-0.4690404 - 0.0982079</td>
</tr>
<tr>
<td>Hub</td>
<td>0.3428</td>
<td>3.1227</td>
<td>0.1100</td>
<td>0.913</td>
<td>-5.777487 - 6.863168</td>
</tr>
<tr>
<td>Biological drugs</td>
<td>0.2648</td>
<td>0.5262</td>
<td>0.5000</td>
<td>0.615</td>
<td>-0.7665649 - 1.29609</td>
</tr>
<tr>
<td>Return on equity</td>
<td>0.0393</td>
<td>0.0252</td>
<td>1.5600</td>
<td>0.119</td>
<td>-0.0100879 - 0.088649</td>
</tr>
<tr>
<td>constant</td>
<td>0.2302</td>
<td>4.0275</td>
<td>0.0600</td>
<td>0.954</td>
<td>7.663514 - 8.123996</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post estimation test</th>
<th>What test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underidentification test (Anderson canon. corr. LM statistic):</td>
<td>14.555</td>
</tr>
<tr>
<td>Chi-sq(1) P-val</td>
<td>0.0001</td>
</tr>
<tr>
<td>Sargan statistic (overidentification test of all instruments):</td>
<td>0.000</td>
</tr>
<tr>
<td>(equation exactly identified)</td>
<td></td>
</tr>
<tr>
<td>Hor: Disturbance is homoskedastic</td>
<td>Pagan-Hall general test</td>
</tr>
<tr>
<td>Chi-sq(8) P-value</td>
<td>0.8127</td>
</tr>
</tbody>
</table>

We suspect that core divestments may not be similar across firm with different values of biologic drugs in development. Thus we create an interaction term by multiplying the values of core divestments counts and biologic drugs in development.
Since we took the square root of the independent variables to transform them, we square the coefficients in the model to back transform them for interpretation.

Results suggest that for a one unit increase in betweenness centrality, the weighted clinical trials count increases by 2262, holding all other variables constant. Since the squared root of betweenness centrality ranges between zero to 0.33, it is more meaningful to say that for a 0.01 unit increase in betweenness centrality, the weighted clinical trials count increases by 22.62, significant at p = 0.027. On average every core divestment is correlated with an 11.55 unit decrease in weighted clinical trials, significant at p = 0.101. Core divestment is not statistically significant at the conventional p=0.05 level. For every unit increase in the interaction term corebio, there is a 0.381 unit increase weighted clinical trial counts, significant at p = 0.0001. Since hub weight ranges from zero to 0.0196, we scale the variable for interpretation. For every 0.001 unit increase in hub weight, there is a 380.964 unit increase in weighted clinical trial counts, significant at p = 0.022.

For every additional year of CEO experience, there is a 0.0344 unit increase in weighted clinical trials. This is not statistically significant (p = 0.913). Compared to firms headed by CEOs with less than the average CEO’s experience in the industry, firms headed by CEOs with more experience are associated with a 0.1175 unit increase of weighted clinical trials. This result is not significant (p = 0.615). For every additional 10% increase of R&D over sales, there is an associated 0.01096 increase in weighted clinical trials. (The calculation is 0.2647624 x log (1.10) = 0.01096.) This result is not significant
(p = 0.615). For every additional unit (dollars per share) increase in return on equity, there is a 0.0015 increase in weighted clinical trials. This result is not significant (p = 0.954).

According to the R-squared, our model accounts for 79.71 percent of the variance in weighted clinical trials. The Anderson Canon test for under-identification indicates that the model is identified. Chi-squared is 0.0001, which is less than 0.05 and we are able to reject the null hypothesis of under-identification. The Sargan statistic suggests that the test of over-identifying restrictions can reject its null hypothesis and that the model is identified (Baum, Schaffer, & Stillman, 2010).
Figure 4 Network analysis of entire network using betweenness centrality
Figure 5 Network analysis of central firms using betweenness centrality

Table 5 Firms with top betweenness centrality scores

<table>
<thead>
<tr>
<th>Firm</th>
<th>Betweenness Centrality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche Holding AG</td>
<td>0.110969815</td>
</tr>
<tr>
<td>Glaxo Wellcome PLC</td>
<td>0.101422488</td>
</tr>
<tr>
<td>Rhone-Poulenc</td>
<td>0.057983873</td>
</tr>
<tr>
<td>Aventis</td>
<td>0.057832062</td>
</tr>
<tr>
<td>Abbott</td>
<td>0.042277032</td>
</tr>
<tr>
<td>Famar SA</td>
<td>0.040306119</td>
</tr>
<tr>
<td>Company</td>
<td>Betweenness Centrality</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>King Pharmaceuticals Inc</td>
<td>0.040230542</td>
</tr>
<tr>
<td>Bristol-Myers Squibb Company</td>
<td>0.03647043</td>
</tr>
<tr>
<td>Pfizer</td>
<td>0.035930777</td>
</tr>
<tr>
<td>Teva Pharmaceutical Industries</td>
<td>0.03241261</td>
</tr>
<tr>
<td>Bayer</td>
<td>0.03099308</td>
</tr>
<tr>
<td>Novartis</td>
<td>0.028941661</td>
</tr>
<tr>
<td>Dura Pharmaceuticals Inc</td>
<td>0.027871756</td>
</tr>
<tr>
<td>Galen Holdings PLC</td>
<td>0.027179406</td>
</tr>
<tr>
<td>Sigma Co Ltd</td>
<td>0.020366318</td>
</tr>
<tr>
<td>Pharmacia Corp</td>
<td>0.019847795</td>
</tr>
<tr>
<td>Insight Pharmaceuticals Corp</td>
<td>0.015400919</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>0.014392461</td>
</tr>
<tr>
<td>Wyeth</td>
<td>0.014233092</td>
</tr>
</tbody>
</table>

Results of the network analysis show a visual pattern in the divestment network. The divestment network shows there are firms central to the network and firms that are peripheral. On the peripheral, there is a ring like pattern created mostly by firms with only one divestment to one other firm. A few of the firms on the peripheral have two or three divestments. The list of the firms with the highest betweenness centrality values shows that divestments are carried out by predominantly the large, brand name pharmaceutical companies that are well known. By revenue, Pfizer, Roche, Abbott, Teva, Bayer, Novartis Laboratories, Eli Lilly and Bristol-Myers Squibb are among the top 12 largest pharmaceutical companies in 2012 and they are also firms with the highest betweenness centrality scores in this study ("Fortune 500 2012: Industry: Pharmaceuticals," 2012). This result supports our argument that the largest brand name pharmaceutical companies are the brokers at the center of divestment deals.
Roche and Galaxo Welcome have the highest betweenness centrality values. Having a higher betweenness centrality score means being able to act as an intermediary for other firms in deals. As Wang finds in her study of knowledge networks in the pharmaceutical industry using mergers and acquisitions data, we also find with divestments data that firms with high betweenness centrality scores are “knowledge hubs” (Wang, 2012: 40). Knowledge hubs are entities through which information flows and most deals are made. In our results, there is a positive relationship between betweenness centrality and innovations that is statistically significant. The divestment network supports our theory that large, brand name pharmaceutical companies are knowledge brokers that can produce innovations through divestments.
5.01 Discussion of results

Our results provide support for the validity of our model and theory. With one exception, all of the coefficients of the independent variables take the expected sign. We measure managerial capabilities using two variables, a dichotomous variable (CEO) and a continuous variable (CEO tenure). Managerial capabilities do not take the expected sign as measured by CEO but does take the expected sign as measured by CEO tenure. Since both are not statistically significant, we reason that a larger sample size with fewer missing data on executive management experience may resolve measurement issues and reconcile the differences in results.

On average, every core divestment is associated with an 11.55 unit decrease in weighted clinical trials. The decrease is expected and our results support the intuitive riskiness of divesting core business to innovations. The core business of large brand-name pharmaceutical companies is developing innovative drugs for human consumption. The core business is important because they house the companies’ core capabilities. For this research-intensive industry, R&D is its core business because R&D is the engine that has traditionally driven innovations (Kester, 2009). For every unit increase in the interaction term corebio, there is a 0.381 unit increase in weighted
clinical trial counts, significant at p = 0.0001. Developing biologic drugs is a new skill for pharmaceutical companies simply because biologic drugs are newer inventions compared to the traditional small molecular drugs. Together, the results suggest that pharmaceutical companies that have more biologic drugs in development may be able to better offset the loss of innovations from core divestments. Next, we explain the results of how knowledge brokering capabilities moderate the relationship between core divestments and innovations.

As expected, there is a positive relationship between divestment capabilities, as measured by betweenness centrality and innovations. Betweenness centrality is defined as the number of times a firm is in the geodesic path between two other firms. Betweenness centrality is based on the premise that firms that can go between other firms in transactions have power (Hanneman & Riddle, 2014). Since we derived the betweenness centrality variable from a divestment network, power in this case is in the form of divestment capabilities. On average, for a 0.01 unit increase in betweenness centrality, the weighted clinical trials count increases by 22.62 units, significant at the p=0.05-level. The results suggest that divestment capabilities help firms innovate via knowledge brokering.

There is a positive relationship between divestment capabilities, as measured by hub weights, and innovations. In the language of network analysis, hubs are entities that point to good authorities. In this study, authorities are buyers of many divested business units. Higher hub weights suggest that a firm is good at directing divestment deals to
authorities. For every 0.001 unit increase in hub weight, there is a 380.96 unit increase in weighted clinical trial counts. This result is statistically significant at the 0.05-level. The results suggest that firms that are good at directing divestment deals to authorities are better knowledge brokers because they produce more innovations. One possible explanation for this is that firms with higher hub weights have deeper knowledge about authority firms such that they are able to direct other firms towards divestment relationships that create more value. Firms with higher hub weights may understand how to direct sellers based on buyers’ medicinal specialties and experience. By directing other firms to authorities, firms with higher hub weights may be reducing information asymmetries between seller and buyers in divestment deals. Our results suggest that divestment capabilities, as measured by hub weights moderate the negative relationship between core divestments and innovations.

The coefficient for absorptive capabilities as measured by R&D over sales takes the expected positive sign but is not statistically significant. The positive relationship between R&D over sales and innovations suggests that conducting internal R&D is important to the ability to source information from outside of the firm. Given R&D over sales has been an established measure of absorptive capabilities in other studies of innovation we believe our insignificant result may be influenced by limited data on the variable (Flatten, Engelen, Zahra, & Brettel, 2011). A larger sample size would likely produce significant results in future studies of the pharmaceutical industry.
A previous study by Grimpe and Kaiser (2010) established a u-shaped relationship between outsourcing and innovations among a sample of firms in multiple industries (Grimpe & Kaiser, 2010). It would be fruitful for future studies to establish the relationship between outsourcing R&D and absorptive capabilities within the pharmaceutical industry. At what level of outsourcing R&D would a research intensive firm reach its tipping point in the pharmaceutical industry? It is reasonable to assume a certain level of internal R&D is required in order to maintain absorptive capabilities because the ability to identify good research partially depends on the ability to conduct research.

We contribute to the literature by filling a literature gap in the important but understudied area of pharmaceutical divestments. The strength of our study is the use of weighted clinical trials, which is a good proxy for innovations that is marketable. Our calculation of the weights is also theoretically sound and practical because they are based on the average pass rates for each phase. Another strength of our study is the pains we take to distinguish between core and noncore divestments for each divestment. This method is likely more reliable than the more common method of using SIC codes, which are dated and nonspecific or NAICS codes that cover broad categories (“Standard Industry Codes,” 1987).
5.02 Limitations

There are limitations to our study. First, we are not able to obtain sufficient data to create a panel dataset, so we are not able to track the performance of each firm over time. We are limited to a cross sectional analysis for this study. Second, our dependent variable, weighted clinical trials count is calculated based on an average pass rates for each phase. This method does not take into account differences in medicinal specialties between firms. Firms chose their own specialties. On average the FDA approved only 16 percent of all drugs entering clinical trials, ranging from a respectable 27 percent for anti-infectives to merely eight percent for neuropharmacologic drugs and seven percent for cardiovascular drugs. There may be a bias in that firms with more capabilities, including more managerial capabilities, chose to pursue more difficult candidate drugs. For instance, managerial capabilities are likely required to handle the lower patient enrollment and retention rates of more challenging specialties such as anti-psychotic drugs (Kaitin, 2010). Thus, if more capable firms chose to specialize in more risky candidates with lower pass rates, then our method may undercount their innovations. In addition, the lag time in this study may also fail to capture innovations that took longer periods of time to reach clinical trials.

On the other hand, our dependent variable may be bias in the opposite direction. Large pharmaceutical companies chose more challenging candidate drugs that are also often in crowded markets because of the higher payoffs. Examples are the overcrowding of the drug markets for hypertension, arthritis, hypercholesterolemia and
depression by many similar drugs (Kaitin, 2010). From this perspective, specializing in more difficult candidate drugs in crowded markets also means focusing on incremental innovations. Thus, from this perspective, our method may overestimate the innovations produced by these firms.

5.03 Conclusion

Our results suggest that the current trend in divestments in the pharmaceutical industry hurts innovations by reducing weighted clinical trial counts but this relationship is moderated in the opposite direction by knowledge brokering capabilities. Our results bear implications for companies, managers and the pharmaceutical industry.

Considering the positive relationship between hub weights and innovations, it may be fruitful for smaller divesting firms to form relationships with firms that are connected to many acquisitioning firms. Forming these relationships may lead to divestments that create more value in terms of producing candidate drugs that can pass pre-clinical testing and reach clinical trials. For small biotechnology firms, forming relationships with large brand name pharmaceutical companies may be especially fruitful for this purpose. Not only can large pharmaceutical firms help small biotechnology firms to shepherd candidate drugs through the FDA approval process, they can also help broker deals.

In the pharmaceutical industry, each new generation of products finances the R&D of the next generation of drug candidates. A failure to innovate imposes penalties against future R&D investments (Kaitin, 2010). For this reason, a steady stream of
innovations is especially important to public health and public policy. Pharmaceutical companies are divesting as a reaction to patent expirations but they are not exiting from the business of producing innovations. Our results suggest that the pharmaceutical industry is moving away from the traditional business model of producing knowledge in-house. The industry’s reaction to expiring patents is to externalize R&D risk via core divestments. The new business model relies more on sourcing knowledge from outside of the firm within knowledge networks. This move to a different business model is an adaptive strategy for firm survival that reflects the collaborative nature of contemporary scientific research. Merck published in its 2000 annual report conceding that it contributed to a mere one percent of the global biomedical research (Gassmann & Reepmeyer, 2005). Firms need to successfully absorb information from the environment outside of their own institutions.

Knowledge brokering via divestments is a way that large brand-name pharmaceutical companies can simultaneously exploit their managerial capabilities and absorptive capabilities. There is always a tension between exploration and exploitation for firms (Duane Ireland & Webb, 2007). Divesting core business via knowledge brokering is a way to explore emerging scientific opportunities while exploiting what large firms do well, managing the complicated FDA approval process. As long as pharmaceutical companies produce innovations, sourcing knowledge from outside of the firm benefits public health.
Our results also bear implications for the federal government. The positive relationship between divestment capabilities and innovations creates room for the government to assist knowledge brokers. Knowledge brokering creates value and the government can provide platforms for firms to collaborate and exchange information. A promising example of the government providing a platform for industry is the partnership between the National Institutes of Health (NIH), 10 large pharmaceutical companies and seven nonprofit organizations. As part of this five-year $230 million partnership, the NIH will host regular information sharing conference calls, meetings and data exchanges, and ultimately release their findings and data for public use. The partnership’s goal is to find molecular targets for the treatment of four elusive diseases that many large pharmaceutical companies are interested in but have not been able to tackle alone: Alzheimer’s disease, Type 2 diabetes, rheumatoid arthritis and lupus (Kolata, 2014).

The partnership is brought about by the change in the technological environment, namely advances in molecular biology generating overwhelming amounts of information that cannot be analyzed by any single firm. Mickael Dolsten, president of worldwide research at Pfizer admits that the partnership would have been inconceivable just five years ago when firms believed they were capable of innovating alone. Now Dr. Dolsten describes innovating as process in which “it is almost like you are traveling in a landscape of biology, but there are no clear signposts of where to go (Kolata, 2014: 1)”. The quote implies that these signposts are outside of the firm.
Without exchanging information and sourcing knowledge from outside of the firm, large, brand name pharmaceutical companies could not innovate effectively. Francis Collins, the director of the NIH announced the unique partnership as “getting together in a way that has not happened before (Kolata, 2014: 1)” This unprecedented partnership illuminates the ongoing need for the government to assist large, brand name pharmaceutical companies to broker knowledge. This partnership is devoted to only four diseases so there is room for the government to form similar partnerships that will address other elusive diseases, such as the many types of cancer.
CHAPTER SIX PUBLIC POLICY IMPLICATIONS OF DIVESTMENTS

6.01 Background

Numerous studies have assessed the impact of proposals for price control on R&D in the pharmaceutical industry. Studies generally agree that price controls would reduce R&D spending in the pharmaceutical industry (Abbott & Vernon, 2007; Giaccotto, Santerre, & Vernon, 2005; Lichtenberg, 2007). If firms are making investment decisions by weighing marginal costs versus marginal benefits, then there is a theoretical reason for the threat of price controls to reduce R&D spending.

Results from studies suggest of reductions in potential innovations across the pipeline as a response to price controls. Calculating net present value is one way for firms to decide whether to proceed with a research project. Using net present value, Abbott and Vernon (2007) predict the impact of price controls on R&D investment at early stage research. The authors’ results suggest that a 40 to 50 percent reduction of prices as part of a price control could reduce phase one clinical trials by 30 to 60 percent (Abbott & Vernon, 2007). Using the number of chemotherapy drugs produced and scientific publications by firms, Lichtenberg (2007) find that a 10 percent decrease in drug prices would lead to a six percent decrease in innovations (Lichtenberg, 2007).
6.02 Research question on policy

R&D is an investment in the pharmaceutical industry that is sensitive to threats. Compared to actual policy changes, policy threats in the pharmaceutical industry have not been studied as thoroughly. One type of threat is the policy uncertainty created by the introduction of Congressional bills that may reduce profits. The bill of interest in this study is the Health Security Act of 1993, which did not pass. The Health Security Act introduced price controls on patented drugs by granting a government committee the authority to set price ceilings for new drugs (McDermott, 1993). At the time of the bill’s consideration, the supply and demand in the market set drug prices in the U.S..

Kutyavina (2010) examined the effect of the mere threat of price controls on the investment decisions of private firms. Her study concluded that the mere threat of legislating price controls reduced R&D spending for firms that sold the majority of their drugs in the U.S. A strong point in Kutyavina’s methodology was the inclusion of firms that did no sell the majority of their drugs in the U.S. as a control group, which increased R&D spending after 1993 (Kutyavina, 2010). With regard to R&D decisions, the results of Kutyavina’s study illustrated just how sensitive firms are to policy threats in the pharmaceutical industry. The results of her study beg the question whether the mere threat of legislation impacts other R&D decisions, especially more permanent decisions by firms.
6.03 Methodology

This study examines the change in divestment networks associated with the introduction of the Health Security Act of 1993. We focus on divestment of core business, which is externalizing R&D and whole disease areas in novel human medicine. A policy threat is defined as a piece of proposed legislation that does not ultimately become public law. The SDC Platinum Mergers and Acquisitions database by Thomson Reuters is used. Firms are selected if they are defined to be part of either the pharmaceutical or biotechnology industry. There is a range of diversification among the firms in our dataset, including firms that do not generate most of its revenue from drug sales, such as Proctor and Gamble to firms that do, such as Merck. Data points are included only if they have divestitures that were affirmed and deal statuses listed as complete. We exclude data points with acquirers listed as “investors”, “investor group” or undisclosed and missing or data with unknown ultimate parent primary ticker symbols.

This study compares the divestment network five years before 1993 (1988-1992) to the divestment network five years after 1993 (1994-1998). Network analysis is performed using Gelphi software version 8.2. Preference settings of visualizations for before and after networks are the same to allow for accurate comparison.

This study visualizes divestment networks using betweenness centrality. Betweenness centrality is defined as the number of times a firm is in the geodesic path between two other firms. Mathematically it is defined as $C_B(i) = \sum_{j \neq k} g_{jk}(i) / g_{jk}$. 

95
The term \( g_{jk}(i) \) represents the number of these geodesics that pass through node \( i \) and the term \( g_{jk} \) represents the number of geodesics linking firms \( j \) and \( k \). Betweenness centrality is based on the premise that firms that can go between other firms in transactions have power (Hanneman & Riddle, 2014). We expect a change in divestment network before and after 1993. We also expect that more dominant firms with top betweenness centrality scores will be large, brand name pharmaceutical companies.

6.04 Results
The network analysis shows a pattern in which there are firms that are central to the network and firms that are peripheral. The firms that are central are connected to many other firms via divestments. The firms on the periphery are connected to only one or two other firms. Next we take a closer look at the firms that are central to the network.
Figure 7 Divestment network of central firms before 1993

Table 6 Firms with top betweenness centrality scores before 1993

<table>
<thead>
<tr>
<th>Label</th>
<th>Betweenness Centrality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roberts Pharmaceutical Corp</td>
<td>428</td>
</tr>
<tr>
<td>SBH (Sally Beauty Holdings)</td>
<td>404</td>
</tr>
<tr>
<td>PG (Proctor and Gamble)</td>
<td>269</td>
</tr>
<tr>
<td>Upjohn Co</td>
<td>239</td>
</tr>
<tr>
<td>Medeva PLC</td>
<td>239</td>
</tr>
<tr>
<td>EK (Eastman Kodak)</td>
<td>134</td>
</tr>
<tr>
<td>GLX (Glaxo Wellcome)</td>
<td>134</td>
</tr>
<tr>
<td>MTC (Monsanto)</td>
<td>133</td>
</tr>
<tr>
<td>ICI (Imperial Chemical Industries)</td>
<td>111</td>
</tr>
<tr>
<td>RHON (Rhône-Poulenc)</td>
<td>97</td>
</tr>
<tr>
<td>Johnson &amp; Johnson/Merck Co</td>
<td>80</td>
</tr>
<tr>
<td>Ciba-Geigy AG</td>
<td>45</td>
</tr>
<tr>
<td>DD (Dupont)</td>
<td>35</td>
</tr>
<tr>
<td>BMY (Bristol- Meyers Squibb)</td>
<td>33</td>
</tr>
<tr>
<td>Seton Healthcare Group PLC</td>
<td>33</td>
</tr>
<tr>
<td>RCOL (Rain Industries)</td>
<td>17</td>
</tr>
</tbody>
</table>
Firms that are central to the divestment network are dominant dealmakers and knowledge brokers because they can go between other firms. Since they are in the geodesic paths of other firms, firms central to the network have the ability to control information flow. Among the firms with the top betweenness centrality scores are Glaxo Wellcome, Rhone-Poulenc, Johnson and Johnson, Merck, Ciba-Geigy, Bristol-Meyers Squibb and Rain Industries, all of which are well known large, brand name pharmaceutical companies. We also note that among the firms with the top betweenness centrality scores are more diversified companies that have pharmaceutical businesses such as, Sally Beauty Holdings, Proctor and Gamble, Monsanto and Dupont.
Figure 8 Divestment network after 1993
Figure 9 Divestment network of central firms after 1993

Table 7 Firms with top betweenness centrality scores after 1993

<table>
<thead>
<tr>
<th>Label</th>
<th>Betweenness Centrality</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFAG (Hoechst)</td>
<td>2123</td>
</tr>
<tr>
<td>GLX (Glaxo Wellcome)</td>
<td>2101</td>
</tr>
<tr>
<td>Holliday Chemical Holdings PLC</td>
<td>1244</td>
</tr>
<tr>
<td>Seton Healthcare Group PLC</td>
<td>1220</td>
</tr>
<tr>
<td>Roussel-Uclaf SA</td>
<td>1050</td>
</tr>
<tr>
<td>DOW</td>
<td>1007</td>
</tr>
<tr>
<td>SBH (Sally Beauty Holdings)</td>
<td>994</td>
</tr>
<tr>
<td>ICN Pharmaceuticals Inc</td>
<td>966</td>
</tr>
<tr>
<td>Company</td>
<td>Betweenness Centrality</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Roberts Pharmaceutical Corp</td>
<td>936</td>
</tr>
<tr>
<td>PG (Proctor and Gamble)</td>
<td>917</td>
</tr>
<tr>
<td>ROG (Roche)</td>
<td>717</td>
</tr>
<tr>
<td>Chiron Corp</td>
<td>644</td>
</tr>
<tr>
<td>Bristol-Myers Squibb Co</td>
<td>474</td>
</tr>
<tr>
<td>MRK (Merck)</td>
<td>407</td>
</tr>
</tbody>
</table>

The divestment network after 1993 shows a pattern in which there are firms central to the network surrounded by firms that are peripheral. Most of the firms that are on the periphery of the network have only two or three divestments with another firm. The central firms are the dominant entities for divestment deals because they can go between other firms and control information flow as knowledge brokers.

There are differences in the divestment network before and after 1993. When we compare the top firms before and after 1993 in terms of betweenness centrality, we notice that more of the dominant knowledge brokers are brand name pharmaceutical firms after 1993. Before 1993, more diversified companies that have pharmaceutical businesses such as Sally Beauty Holdings, Proctor and Gamble, Monsanto and DuPont were among the tops firms in terms of betweenness centrality scores. After 1993, there are only three diversified firms among the top firms in terms of betweenness centrality scores. Most divestments are core divestments. Our results suggest that after the policy threat, brand name pharmaceutical companies took more central positions in the divestment network.
6.05 Discussion and limitations

Even when proposed legislations do not pass the Congress and fail to be enacted into law, they have an impact on innovations because pharmaceutical firms react to policy threats. The Health Security Act of 1993 was publicized by President Bill Clinton on September 22, 1993. The main limitation of our study is that we could not control for other factors that influence divestment networks, such as industry wide trends or economic cycles.

Kutyavina’s study showed that the threat of legislation did not reduce R&D expenditure among the largest firms but only among firms that were less innovative (Kutyavina, 2010). In our study, we find that large pharmaceutical companies are knowledge brokers in divestment networks and that more pharmaceutical companies ranked the top of the list in terms of betweenness centrality scores after 1993. Thus, legislative threats that mainly affect smaller, less innovative firms may produce more muted or subtle changes in divestment networks in which larger firms play the central role.

Another limitation of our study is the realness of the legislative threat as perceived by the pharmaceutical industry at the announcement of the bill. As a large stakeholder in public policy, the pharmaceutical industry engages in heavy lobbying and has access to inside knowledge of proposed legislations before the bills become public (Kutyavina, 2010; Levinthal, 2013). Thus, based on inside information the pharmaceutical industry may have been able to predict that the bill was very unlikely to
pass. Had the industry perceived the unlikeliness of the threat coming into fruition, it
would not have reacted to the threat or at least not as severely as if the threat was
more real.

Lastly, divestment networks are the product of deals, which are more
pronounced reactions than R&D reductions. Deals are more permanent and less able to
be reversed than changes in short term expenditure. Thus, a policy threat may produce
a less noticeable reaction in divestment networks.

Companies usually calculate net present value of a project when deciding
whether to proceed to fund it. A project with a positive net present value suggests a
positive return on investment. A project with a negative net present value suggests a
loss. Drug companies prefer to invest in innovations with a positive net present value
(Reed, Califf, & Schulman, 2006). Legislators should consider the effects of bills on the
net present value of R&D projects. The effect of legislative threats to the R&D decisions
of firm is an understudied area that is important to public policy and public health.

Given the deliberative nature of the U.S. Congress and the controversial issues of
drug prices/ reimbursement, many more bills are likely to be introduced and publically
debated. The aging population will demand for more pharmaceutical solutions to
chronic diseases. And health reform efforts such as those reshaping Medicare, Medicaid
and private insurance will likely require national dialog and debates among many
stakeholders (AHRQ, 2002). This sets the stage for many policy threats that will
ultimately not pass to be considered and the Congress should take into account the
effects of mere policy threats to R&D decisions by firms. To the pharmaceutical industry, each bill is a potential policy threat that may need to be addressed by new R&D decisions and recalculation of net present values of projects. Biotechnology firms would be especially sensitive to the adverse effects of regulatory changes because they are very dependent on external venture capital funds. And since biotechnology firms specialize in developing biologic drugs that are more promising than traditional small molecular drugs, the Congress should be especially thoughtful when introducing bills that disproportionately impact this sector of the drug industry (PriceWaterhouseCoopers, 2009). These results suggest that the FDA should take effects on innovation into account when calculating the risks and benefits of a proposed regulatory change.


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BIOGRAPHY

Rebecca Mao graduated from Haverford College in 2005 with a Bachelor of Science majoring in (molecular) biology. She earned her Master of Public Health from the George Washington University in 2007. She completed the Presidential Management Fellowship in 2009.