# Decoding the Adaptability-Rigidity Puzzle: Evidence from Biopharmaceutical Incumbents' Pursuit of Gene Therapy and Monoclonal Antibodies

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## ABSTRACT

The emergence of radical technological regimes renders obsolete the value of incumbent firms' existing competences and presents a significant challenge to their long-term sustainability. We explore when incumbents' investments in radical technologies may facilitate adaptation and when they may succumb to the forces of organizational inertia. Our theoretical framework accounts for the possibility that incumbents may invest in new technologies through a variety of modes (internal research, external research contracts, research alliances and acquisitions) and that a radical technology may not conform to the incumbents' prevailing business models. This lack of fit with the existing business model is an important source of organizational rigidity associated with the incumbent's commercialization of new technologies. We consider how the different modes of pursuing a new technology differ in the extent to which they are shielded from incumbents' inertial pressures. We argue that this difference helps explain why incumbents, despite investing in radical technologies, may still be unable to navigate technological change, and what types of investments will be more effective in achieving desired commercialization outcomes. Evidence from biopharmaceutical incumbents' investments in Monoclonal Antibodies and Gene Therapy from 1989 to 2008 offers strong support for our framework.

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## INTRODUCTION

The emergence of radical technological regimes renders obsolete the value of incumbent firms' existing competences and presents a significant challenge to their long-term sustainability (Cooper & Schendel, 1976; Tushman & Anderson, 1986; Hill & Rothaermel, 2003). Incumbents have been shown to successfully adapt if they invest in new technologies and possess complementary assets that are necessary for the technology's commercialization (e.g., Tripsas, 1997; Rothaermel, 2001; Nicholls-Nixon & Woo, 2003; Eggers & Kaplan, 2009). Yet established firms such as Kodak, NCR, and Polaroid, despite investing in new technologies and having access to complementary assets, faced great difficulties in managing technological change (e.g., Rosenbloom, 2000; Tripsas & Gavetti, 2000; Christensen, 2006). In this study, we shed light on this puzzle by explaining when incumbents' well-intended investments in a radical technological regime are likely to facilitate adaptation and when they may succumb to the forces of organizational inertia.

We examine incumbents' management of technological change by separating upstream actions geared towards creation of new knowledge (invention) from downstream actions geared towards the commercialization of new knowledge (innovation) (Freeman & Soete, 1997). Studies of radical technological change have tended to focus on incumbents' competence destruction and on the challenges of new knowledge creation. Somewhat less explored are challenges of knowledge commercialization because of new technologies not conforming to the incumbents' prevailing business models of how they generate revenues and appropriate profits (Abernathy & Clark, 1985; Christensen, 2006; Wu, Wan, & Levinthal, 2013). Similarly, the locus of new knowledge creation has traditionally been viewed through the incumbent's internal research unit (Henderson, 1993; Christensen & Bower, 1996; Kaplan & Henderson, 2005). Beyond the internal research unit, incumbents increasingly access and build on knowledge from

entrants and research organizations through the use of research contracts, research alliances and technology acquisitions (Rothaermel, 2001; Nicholls-Nixon & Woo, 2003; Anand, Oriani, & Vassolo, 2010).

In this study, we account for the possibility that in addition to supply-side competence destruction, a radical technological regime may *ex ante* lack the demand-side fit such that some new technologies may sustain while others may disrupt incumbents' business models (Abernathy & Clark, 1985; Christensen & Raynor, 2003). The lack of demand-side fit is an important, but as yet underexplored, source of organizational rigidity associated with incumbents' commercialization of new technologies. We argue that while incumbents invest in new technologies, the technology's commercialization may still be subjected to organizational inertia stemming from their routines, cognition and resource dependencies (e.g., Rosenbloom, 2000; Tripsas & Gavetti, 2000; Gilbert, 2005). We offer a theoretical framework that considers how the different ways of pursuing a new technology (i.e., internal research unit, external research contracts, research alliances, acquisitions) differ in the extent to which they are shielded from incumbents' inertial pressures. The framework explicates the relationship between incumbents' investments and commercialization for sustaining and disruptive technological regimes.[1] In so doing, we are able to show why firms, despite investing in new technologies and having access to complementary assets, may still be unable to manage technological change, and what types of investments will be more effective in overcoming organizational rigidity and achieving desired commercialization outcomes.

[1] In this study, we use the phrase "technological regime" to refer to specific knowledge bases and/or procedures as solutions to relevant problems within a given context (Dosi, 1982; Nelson & Winter, 1982; Anderson & Tushman, 1990). While "technology" may sometimes be confounded with a physical artefact (e.g., steamships, cell phones), technological regime provides greater generalizability and is much more consistent with our empirical context (e.g., Pisano, 1990; Nicholls-Nixon & Woo, 2003).

The context for the study is the global biopharmaceutical industry from 1989 to 2008, a period during which the industry witnessed the emergence of two of the most revolutionary therapeutic approaches based on genetic engineering – Monoclonal Antibodies (MAbs) and Gene Therapy (GT). Hundreds of biotechnology entrants pursued these radical technologies in the hope of altering the industry landscape (Schweizer, 2005; Pisano, 2006; Sosa, 2012). A critical aspect of the research context was that while incumbent firms' had access to the specialized complementary assets such as capabilities in clinical development, relationships with healthcare service providers and sales force that are required for the commercialization of both MAbs and GT, the two regimes differed in the extent to which each conformed to the incumbents' prevailing business models. MAbs sustained the existing business model of incumbent firms (i.e., long term treatment often administered at home resulting in yearly treatment costs for patients and insurers) while GT was much more disruptive (i.e., typically one-off or significantly less frequent treatment administered by the physicians). Hence, the traditional business model based on regular prescriptions is less applicable to gene therapy (Dubois, 2012; Wilson, 2012). Incumbents responded to the emerging technological regimes by investing in both MAbs and GT. These investments were directed towards their internal research units as well as towards biotechnology entrants and research organizations through the use of research contracts, alliances and acquisitions.

We assembled a unique panel dataset that included information on incumbents' technology investments and commercialization attempts for MAbs and GT over the course of approximately two decades. In so doing, we are able to clearly disaggregate incumbents' activities geared towards invention and those geared towards innovation (Freeman & Soete, 1997). We also conducted semi-structured interviews with 14 senior industry professionals with

direct experience in the research and commercialization of MAbs and GT so as to develop an in-depth understanding of our empirical context and to corroborate our findings.

We found that while incumbents' investments in internal research and contract research increased their likelihood of commercialization of MAbs, no such effect was found for GT. In contrast to investments in internal and contract research, those in research alliances and acquisitions had a significant effect on the commercialization for GT. These results suggest that commercialization of knowledge underlying a radical technological regime that does not conform to the prevailing business model is subject to incumbent inertia, and that different modes of investments vary in the extent to which they are shielded from rigidity-inducing organizational processes. In our interviews, industry participants offered several valuable insights that helped to shed light on the key mechanisms underlying these findings.

To the best of our knowledge, this study is a first attempt to systematically identify the different organizational modes by which incumbents may invest in radical technological regimes while accounting for the possibility that beyond supply-side competence destruction, radical technological regimes may also lack the demand-side fit with the incumbents' business models. In so doing, we are able to offer a framework that introduces new organizational and strategic contingencies to explain when incumbents' investments in an emerging technological regime are likely to yield desired commercialization outcomes. By showing that different types of adaptive investments toward the generation of new knowledge can be subject to different levels of rigidity in the commercialization of new knowledge, the study reaffirms the value of moving beyond adaptability vs. rigidity to how these elements are intertwined during episodes of technological change. Second, the observed difference in the impact of external research contracts and alliances on the likelihood of commercialization for GT highlights an important distinction

between incumbents' actions and decisions. While in both cases, incumbents act to draw on new knowledge beyond their boundaries, unilateral market-based and bilateral alliance-based arrangements differ in the extent to which the decisions regarding commercialization are externalized and hence, in the extent to which they could be shielded from the internal rigidity-inducing organizational processes. Third, our findings also help clarify a frequent misconception regarding the disruptive technological regime, which is that incumbents do not invest in such a regime. As documented in several studies (Christensen & Bower, 1996; Sull, Tedlow, & Rosenbloom, 1997; Tripsas & Gavetti, 2000; Gilbert, 2005), incumbents often do invest in such regimes. However, as our results show, many of such initial research investments may not lead to subsequent commercialization. This suggests that the locus of incumbent inertia is not necessarily at the point of investment but rather at the point of commercialization, and that research alliances and acquisitions may offer a means to overcome that inertia. Finally, by considering distinct technological regimes that emerged within the broad biotechnology field, we are also able to explain the lack of support found in earlier studies regarding the commercialization implications of incumbents' research investments (Rothaermel, 2001; Nicholls-Nixon & Woo, 2003). For example, despite arguing that incumbents' investments in internal research and those directed towards external research contracts and alliances will lead to new products, Nicholls-Nixon and Woo (2003) did not find support for such a relationship. Our results suggest that more clarity on this relationship can be gained by disaggregating the broad biotechnology field into specific technological regimes, and by characterizing how they interact with the incumbents' organizational and strategic context.

## THEORY AND HYPOTHESES

The emergence of radical technological regimes presents a significant threat to the sustainability of industry incumbents. Such regimes entail novel methods and materials that are derived from entirely different knowledge domains as those of established firms (Freeman & Soete, 1997; Hill & Rothaermel, 2003). A large body of literature has examined how radical technological change impacts incumbents. Earlier studies emphasized entrenchment in the existing technology and the failure to invest in the emerging technology (Cooper & Schendel, 1976; Foster, 1986; Utterback, 1994). Recent studies have consistently found incumbents to be more responsive to the threat from the radical technology (e.g., Tripsas, 1997; Rothaermel, 2001; Eggers & Kaplan, 2009). Within this research stream, the adaptability of incumbents in the face of technological change has been attributed to their ability to leverage their specialized complementary assets that are necessary for the commercialization of the new technology. Therefore, investments in radical technologies, coupled with access to specialized complementary assets, are in general theorized to facilitate adaptation (Hill & Rothaermel, 2003). Contrary to this expectation, there are documented cases in which firms despite investing in radical technologies and having access to complementary assets, faced great difficulties in managing technological change (Cooper & Schendel, 1976; Rosenbloom, 2000; Tripsas & Gavetti, 2000). Such empirical irregularities have led to doubts about the external validity of the specific studies and our general understanding of the impact of technological change on incumbents (e.g., Chesbrough, 2001; Christensen, 2006).

In this study, we explore incumbents' management of technological change by distinguishing between efforts with respect to the creation of new knowledge (invention) and those with respect to commercialization of the knowledge (innovation) (Freeman & Soete, 1997).

This disaggregation allows for the possibility that efforts with respect to knowledge creation may not automatically translate to successful knowledge commercialization (Abernathy & Clark, 1985). New technological regimes may present very different commercialization contexts to incumbents. Some regimes may sustain the incumbents' prevailing business model of how they generate revenues and appropriate profits while others may be disruptive such that they are relatively unattractive within the prevailing business model (Abernathy & Clark, 1985; Christensen, 2006; Wu et al., 2013).[2] For example, Tripsas and Gavetti (2000) provide a rich description of how Polaroid undertook significant investments in digital imaging technology. However, Polaroid's razor/blade business model led those investments to be channelled into a digital camera/printer product with which users could print and view their images using Polaroid's instant film (a major source of the firm's profits) rather than viewing them on an LED screen. Moreover, Polaroid's existing business model also constrained the development of related downstream capabilities such as low-cost electronic manufacturing, marketing and sales, contributing to the Polaroid's inability to sustain its success in the new technology landscape. Hence, the difference in the extent to which the radical technology sustains the incumbents' business model is an important source of rigidity underlying the commercialization of new technology.

Similar to the case of Polaroid, scholars have offered additional case-based evidence of incumbents investing in new knowledge but being subject to organizational inertia during the commercialization of that knowledge (e.g., Henderson & Clark, 1990; Leonard-Barton, 1992; Rosenbloom, 2000; Gilbert, 2005). These explorations have considered incumbent rigidity

[2] We note that the characterization of a new technological regime with respect to the incumbent's business model was not present in Christensen's early publications on this topic (e.g., Christensen & Rosenbloom, 1995; Christensen, 1997), but rather was a result of subsequent refinement (Christensen & Raynor, 2003; Christensen, 2006). Note, however, that this characterization has its roots in the earlier seminal paper by Abernathy and Clark (1985) who use the notion of market transilience to describe such an effect.

through the lens of capabilities, incentives, routines, cognition and resource dependencies. While they have generated valuable insights, the locus of inventive activities to create new knowledge is confined to the incumbent's internal research unit. Increasingly, the locus of inventive activity also entails incumbents drawing on and building on knowledge from entrants and research organizations through the use of research contracts, research alliances and technology acquisitions (Rothaermel, 2001; Nicholls-Nixon & Woo, 2003; Anand et al., 2010). Hence, it is important to understand how these different modes of investments may interact with rigidity-inducing organizational processes during the incumbents' pursuit of new technologies.

We develop a framework that explicitly differentiates between radical technological regimes that are sustaining vs. those that are disruptive. We consider incumbent responses to entail investments in internal research, external research contracts, external research alliances and technology acquisitions. The framework predicts when incumbents' investments in radical technologies are likely to result in desired commercialization outcomes and when they may be subject to the forces of organizational inertia. In so doing, we are able to show why incumbents, despite investing in radical technologies and having access to complementary assets, may still be unable to manage technological change, and what types of investments will be more effective in overcoming organizational rigidity.

**Pursuit of Radical Technological Regime and Incumbent Inertia**

Incumbents undertake significant in-house R&D efforts in the face of technological change (Gambardella, 1992). As such, the literature has often theorized and observed incumbents' pursuit of new technology within their internal research units (e.g., Henderson, 1993; Tripsas & Gavetti, 2000; Kaplan, 2008). Internal research investments are tightly coupled

within the existing organizational context. Having invested in the development of new knowledge, when and how such knowledge is commercialized is shaped by the existing incentive structures and cognition of strategic decision makers, as well as the resource allocation organizational processes (Gilbert, 2005; Kaplan & Henderson, 2005).

A sustaining technological regime embraces a firm's existing model of generating revenues and profits, and carries the immediate appeal of translating in-house research investments into commercialization of products (e.g., Christensen & Raynor, 2003). For example, the emergence of wireless telephony represented a case of a sustaining technological regime because it provided wireline telephone companies a higher per-minute rate by building a network along the routes of their most attractive, least price-sensitive customers (Christensen, 2006:49). Having invested in new technology and recognizing the new commercial opportunities within the context of their existing business model, incumbents would have strong incentives to commercialize the technology.

In contrast, a disruptive technological regime represents a case in which the new regime is relatively unattractive within the existing business model of how incumbents create, deliver and capture value. For example, the emergence of minimills represented a case of a disruptive technological regime for integrated steel companies because of their focus on higher-margin segments (sheet steel and structural beam) that could not be addressed by the minimills technology (Christensen, 1997). Similarly, the emergence of radial technology was unattractive to the incumbents in the US tire industry (Sull et al., 1997). As compared to the then existing bias-ply tires, the radial tires had substantially longer life. While the superiority of radial tires for the consumer was well-known (longer wear, better gas mileage, greater safety and better handling), longer life meant a drastic reduction in the number of tires used by an automobile over

its lifetime, and a corresponding decrease in the demand for tires. Moreover, this reduction in demand only affected the replacement market segment, shifting the distribution of tire manufacturers' sales towards the unprofitable original equipment automobile manufacturer segment.

Disruptive technological regimes lack fit with the existing business model, making it more difficult for internal investments to garner additional organizational resources and attention towards technology commercialization. The problem is exacerbated because commercialization tends to be highly routinized in incumbent firms (Henderson & Clark, 1990), and the translation of research investments into commercialization will likely be subject to routine rigidity (Gilbert, 2005). At the same time, the presence of alternative technological solutions may require firms to make trade-offs in their resource allocation as they cannot sponsor all possible development projects (Adner & Levinthal, 2008).

Even though incumbents pursue in-house research investments in disruptive technological regimes, the desire to preserve their existing business models, the internal resource allocation constraints and the rigidity in commercialization routines will subject these investments to organizational inertia. Hence, as compared to internal investments in sustaining technological regimes, those in disruptive technological regimes will lack the impetus to get translated into commercialization. Accordingly, we propose:

*Hypothesis 1: In an emerging technological regime, incumbents' internal research investments will more likely lead to commercialization when the technological regime is sustaining than when it is disruptive.*

Beyond internal research, incumbents draw on entrants and research organizations to access and develop new knowledge underlying new technologies (Pisano, 1990; Rothaermel, 2001). An increasingly common approach is the use of contract research to access new

knowledge domains through markets for technology (Arora, Fosfuri, & Gambardella, 2001). Often, this mode involves incumbents' outsourcing of a given R&D project and/or licensing a specific IP from a start-up or a research organization with the goal of adding new knowledge to the firm (Markman, Gianiodis, Phan, & Balkin, 2005; Leone & Reichstein, 2012). Once the incumbent has secured exclusive or non-exclusive access to the externally developed knowledge, it still needs to subsequently build on and commercialize that knowledge. While investments in contract research shift the locus of invention outside the incumbent's boundary, it preserves the incumbent's organizational context for the commercialization of those inventions. Hence, whether incumbents pursue contract research or internal research, the incentive structures and cognition of managers as it relates to downstream commercialization, as well as the resource allocation processes, remain largely alike. This makes the decisions regarding the commercialization of contract research subject to similar rigidity inducing organizational processes as that of internal research. Moreover, upon commercialization, incumbents make royalty payments to the licensor (Leone & Reichstein, 2012), which can further reduce the incentive to commercialize the emerging technology with an unproven business model. Hence, while contract research has often been proclaimed as a solution for incumbents to manage technological change (Pisano, 1990; Nicholls-Nixon & Woo, 2003), it may not deliver on its promise for disruptive technological regimes:

*Hypothesis 2: In an emerging technological regime, incumbents' investments in contract research will more likely lead to commercialization when the technological regime is sustaining than when it is disruptive.*

So far, we have argued that commercialization of knowledge developed in-house or accessed through contract research is subject to organizational rigidity if the technological regime is disruptive. We next consider how incumbents' investments through research alliances

and acquisitions might be able to overcome such inertial pressures associated with the commercialization of disruptive technological regimes.

**Overcoming Incumbent Inertia**

Bilateral research alliances in which incumbents typically partner with new entrants or universities to jointly pursue research are becoming an increasingly prevalent mode by which incumbents invest in new technologies (Rothaermel, 2001; Anand et al., 2010). Research alliances are distinct from research contracts (Gulati & Singh, 1998; Steensma & Corley, 2000; Gilbert, 2005; Kale & Singh, 2009) In contrast to research contracts which entail a one-off market-based exchange, alliances involve partners pooling resources through a separate organizational entity.[3] Hence, as compared to both internal research and contract research, a research alliance presents a case of an autonomous action by the incumbent that is structurally separated from the internal organization. This structural separation relaxes the constraints imposed by the incentive structures, resource allocation processes and organizational routines within the incumbent organization, and hence, will act to lower the organizational rigidity associated with the commercialization of disruptive technologies (Burgelman, 1983; Christensen & Raynor, 2003; Hill & Rothaermel, 2003; Gilbert, 2005). Research alliance also involves a dedicated decision-making and governance structure which comprise technical and managerial personnel from both incumbent firms and their partners (Steensma & Corley, 2000). Therefore, critical decisions regarding research and commercialization are driven not only by incumbents but also by the outside partners (typically start-ups or research organizations). These partners are

[3] Firms in technology-based industries also form alliances that may not involve research but only commercialization in which a research output of one firm is commercialized by drawing on the complementary assets of the partner firm. While we control for these commercialization-only alliances in our empirical analysis, these are not the focus of our theory.

not subjected to the incumbents' cognitive constraints and have strong incentives to commercialize their research, despite an unproven business model (Gilbert, 2005). Moreover, incumbents' middle managers who are dedicated to governing the research alliance are less impacted by the existing beliefs within the incumbent organization, and are therefore more likely to question the status quo (Burgelman & Grove, 1996; Hill & Rothaermel, 2003; Furr, Cavarretta, & Garg, 2012). By being in contact with outsiders, the managers are also well-informed about the commercialization opportunities underlying disruptive technologies. Finally, given that incumbents share risks and costs with an external partner, they may be more likely to pursue commercialization despite the added uncertainty associated with respect to the business model.

In summary, the pursuit of an emerging technology through a research alliance represents a structurally separated organization with risk sharing and outsider influence on decision making. As compared to incumbents' investments in internal and contract research, those in research alliances will be less impacted by the internal organizational constraints associated with the commercialization of disruptive technological regime. Accordingly, we propose:[4]

*Hypothesis 3a: When pursuing disruptive technological regimes, incumbents' investments in research alliances will more likely lead to commercialization than will investments in internal research.*

*Hypothesis 3b: When pursuing disruptive technological regimes, incumbents' investments in research alliances will more likely lead to commercialization than will investments in research contracts.*

Finally, acquisitions of start-ups represent another important mode by which incumbent firms invest in new technological regimes (Chaudhuri & Tabrizi, 1999; Nicholls-Nixon & Woo,

[4] We note the possibility that, depending on the context, different types of technology investments may, in general, vary in their impact on incumbents' technology commercialization. For example, it is possible that investments in research alliances may more likely lead to commercialization than those in research contracting or internal research for all types of technologies. We account for this possibility in our empirical analysis by including incumbents' investments in sustaining technological regimes as a control.

2003). As compared to internal research, acquisitions offer firms a means of internalizing and building on new knowledge developed by technology start-ups. An important consideration for acquirers to benefit from such acquisitions is to minimise the disruption to the acquired research team and to retain the key inventors and decision makers. Therefore, in their quest to continue making progress in the new technology, acquirers typically preserve the autonomy of the acquired start-ups as structurally separate units (Puranam, Singh, & Zollo, 2003). For example, Schweizer (2005) showed that when biopharmaceutical incumbents acquire biotechnology entrants for new technological capabilities, they tend to grant a high degree of autonomy to the acquired firms. Similarly, Puranam et al. (2009) found that information technology hardware firms were more likely to preserve the structural autonomy of acquired small technology-based firms with standalone technologies. Such a structural separation helps to ensure that the commercialization of knowledge developed within the acquired units is not subject to the incentives, routines and cognitive processes that exist within the parent organization.[5] Hence, acquired research units may be shielded from the incumbent's internal organizational constraints associated with the commercialization of disruptive technologies. In addition to structural autonomy, executives from acquired firms are typically retained and continue to play an influential role in post-acquisition decision making with respect to the new technology (Chaudhuri & Tabrizi, 1999; Ranft & Lord, 2002; Schweizer, 2005). These "outsiders" are not subject to the cognitive constraints of internal managers (Furr et al., 2012). Moreover, they will have strong incentives to commercialize their unit's research output despite a lack of fit with the incumbent's prevailing business model (Gilbert, 2005). Hence, investments in new

[5] Our prediction is premised on the arguments and findings in prior studies (Schweizer, 2005; Graebner, Eisenhardt, & Roundy, 2010) that acquiring firms will preserve the structural autonomy of the acquired start-ups with knowledge and capabilities in new technologies. We confirmed that this premise continues to hold within our dataset and we present the supporting quantitative and qualitative information after presenting our main results.

technological regimes through acquisitions represent the pursuit of the technology through structurally separated research units with decision makers who are less subjected to the cognitive and incentive constraints within the parent organization. Accordingly, we propose:

*Hypothesis 4a: When pursuing disruptive technological regimes, incumbents' investments in technology acquisitions will more likely lead to commercialization than will investments in internal research.*

*Hypothesis 4b: When pursuing disruptive technological regimes, incumbents' investments in technology acquisitions will more likely lead to commercialization than will investments in research contracts.*

## RESEARCH CONTEXT

We explore our arguments in the context of the global biopharmaceutical industry from 1989 to 2008. The inception of biotechnology in the 1980s has been characterized as a radical technological change from chemistry-based to biology-based therapeutic solutions in the pharmaceutical industry. Biotechnology draws on knowledge from genetics and large molecules (proteins) in the human body to develop new types of therapies. Initially, researchers focused on recombinant DNA to produce human therapeutic solutions. The late 1980s saw the next wave of the biotechnology revolution as new therapeutic approaches drawing on genetic engineering started to emerge. We focus on the two approaches that gained the most attention during this period - Monoclonal Antibodies (MAbs) and Gene Therapy (GT). These approaches represent distinct technological regimes as they draw on different knowledge bases within biology and entail very different approaches to treating illnesses (Pisano, 2006). The empirical context provides an ideal setting for the purpose of the study. Both MAbs and GT continued to leverage incumbent firms' key complementary assets such as capabilities in clinical development, relationships with healthcare service providers, and sales force. Both MAbs and GT required

incumbents to invest in new biology-based competences which they did by pursing internal research as well as accessing external know-how through research contracts, alliances and acquisitions. At the same time, MAbs and GT significantly differed in the extent to which they reinforced the incumbents' business model. Finally, this context allows us to systematically trace incumbents' research investments and commercialization attempts for the two technological regimes over a period of approximately two decades.

**Data**

We followed the mixed methods approach of explanatory sequential design (Creswell & Clark, 2011) in which we first conducted a quantitative analysis and followed up with a second qualitative phase to shed light on the mechanisms and to explain the quantitative results in greater depth. For the quantitative analysis, we focused on the largest 50 global publicly traded biopharmaceutical incumbents based on total pharmaceutical revenues in 1991 using Compustat and annual reports.[6] Limiting the sample to the leading firms ensured that we observed the vast majority of incumbents' investments in GT and MAbs and at the same time, facilitated the data collection process across multiple databases. This approach is consistent with prior research examining incumbents' management of technological change (Rothaermel, 2001; Kaplan & Tripsas, 2008; Anand et al., 2010). We excluded firms that focus only on generics or re-formulations and do not compete in the innovative biopharmaceutical market segment. For each firm, we constructed a detailed history of divisions and subsidiaries using the Directory of Corporate Affiliations, LexisNexis and corporate websites. This helped to ensure that the

[6] During the period of the study, there were 12 mergers among firms in the sample (e.g., Astra AB and Zeneca forming AstraZeneca). Such cases were treated as separate firms before the merger and as a single entity after the merger. Also, among the initial sample, there were 5 firms that merged very early on during the period of observation. We replaced these firms in the sample with large biopharmaceutical firms that did not meet the initial Top 50 cut-off based on pharmaceutical sales but which were in the Top 55.

subsidiaries are accounted for within the same corporation. We assembled a unique firm-level panel dataset that included firms' research investments as well as commercialization attempts for both MAbs and GT from 1989 to 2008. Information on firms' research contracts, research alliances and technology acquisitions was obtained from Recombinant Capital (ReCap). ReCap, a proprietary database tracking the life science industry, is considered to be one of the most comprehensive publicly available industry data sources (Schilling, 2009). We used information from incumbents' patent grants to measure their investments in internal research (e.g., Kaplan, 2008). This information was obtained from Derwent World Patents Index database. Finally, information on commercialization was obtained from Pharmaprojects and Adis R&D Insights, both of which have been used in a number of prior studies (e.g.,Adegbesan & Higgins, 2011; Hess & Rothaermel, 2011; Sosa, 2012).

For the qualitative data, we interviewed 14 senior industry professionals to understand the differences between MAbs and GT, and how incumbents pursue these emerging technologies through internal and external research initiatives. These professionals came from a variety of backgrounds (six large incumbents, three biotech start-ups, a university and two dedicated research institutes) with direct experience in the research and commercialization activities of MAbs and GT. The interviews were semi-structured based on an interview guide, lasting an average of 45 minutes. Frequently, we followed up to clarify certain details via emails.

**Emergence of Monoclonal Antibodies and Gene Therapy**

MAbs and GT radically differed from the traditional therapeutic approach using chemical-based solutions. Both technologies required a fundamental understanding of human biology which, according to a senior manager of a large pharmaceutical firm, led to the "decline

of chemists and an emergence of biologists within the drug development process of biopharmaceutical firms."

Antibodies are produced by the human immune system in response to foreign proteins (antigens) that are the cause of illnesses and diseases. Therapies using monoclonal antibodies (MAbs) reinforce the internal immune system and have several advantages over traditional chemical-based treatment. For example, they are much more specific to an antigen, have lower risk of toxicity and can address biological mechanisms that cannot be addressed by traditional chemical-based small molecules(Burns, 2005)(Burns, 2005).

Gene therapy (GT) is based on a revolutionary idea for the treatment of inherited diseases caused by defective genes. The therapy entails inserting corrected genetic material (DNA) into human cells so as to reprogram and restore their functionality in the human body. The new genetic material is inserted through a vector, which delivers the genes to the appropriate cells. Given that the insertion of a "good" gene does not always solve the therapeutic problem, other related methods (e.g., antisense or t-cells) are utilized, which may not repair a damaged gene but may deter it from functioning.

While both MAbs and GT required that incumbents develop new competences in biology-based therapeutic solutions, they profoundly differed in their interaction with the incumbents' prevailing business model. MAbs sustain the industry's existing business model. Similar to traditional drugs commercialized by biopharmaceutical incumbents, MAbs-based drugs can be taken by patients at home (e.g., by intravenous injection using syringes or preloaded pen devices) and are prescribed as a long term treatment, resulting in yearly treatment costs for patients and insurers. A scientist highlighted that MAbs in fact resemble "classic small molecule drug as they are readministered, treat a large percentage of the population and have the

opportunity to make money long term." For example, Humira – the best-selling MAbs drug in 2012 for the treatment of rheumatoid arthritis – is prescribed at a cost of about $20,000-30,000 per year per patient (Miller & Feldman, 2006).

In contrast, treatments based on GT are administered by physicians in hospitals through intramuscular injections or surgical procedures. More importantly, GT-based treatments tend to be one-off or infrequent, which means that the prevailing biopharmaceutical revenue model based on regular prescriptions will not be as applicable. The quote below from a report in *Forbes Magazine* illustrates this disruptive nature of GT:

> "Talk about transforming an industry, Big Pharma has always been pill-based whereas gene therapy is one and done." - George Day, as quoted in Dubois (2012).

A business development manager of an incumbent biopharmaceutical firm also commented on the uncertainty about the business model of GT in our interview:

> "While MAbs have been validated by Wall Street, understanding the business case for Gene Therapy has been something that's been a moving target. And I admit the marketplace does not exactly know what it needs."

Similarly, Wilson (2012) uses the case of hemophilia A & B to discuss the disruptive nature of GT. The traditional treatments for these illnesses are based on regular protein replacement products. GT treatment, predicated on a one-time injection, not only threatens the existing $6.5B protein replacement market but also presents a lack of clarity regarding how such treatments would be priced and reimbursed. A recent case in point is the approval of Glybera by uniQure in Europe for treating lipoprotein lipase deficiency. uniQure and insurers faced significant challenges as to how to price this one-off or less frequent gene therapy-based treatment (e.g., Moran, 2012).

Hence, while both MAbs and GT represent radical technological regimes for biopharmaceutical incumbents, they differ significantly in their interaction with the incumbents' business models. While MAbs sustain the existing business model, GT is much more disruptive.

**Incumbents' Research Investments in Monoclonal Antibodies and Gene Therapy**

*Internal research:* We used the information on firms' patented inventions to observe their internal research investments in MAbs and GT. Derwent categorizes all patents in its database into 21 distinct technology sections, each of which is divided into several classes.[7] Section B is the primary section for biopharmaceutical patents. Classes in Derwent are consistently applied by Derwent's editors. MAbs and GT received dedicated classes in the 1990s that were labeled as monoclonal antibody, gene therapy and gene delivery. To verify the correspondence of Derwent classes with the specific technological regime, we consulted a senior scientist with the University of Pennsylvania's School of Medicine, who confirmed their applicability for the study. Figure 1a plots the trend in the total number of patent grants based on the application date by firms in our sample. Incumbents invested in both MAbs and GT. While investments in MAbs exhibited a head start in the early 1990s (1991-1993), investments in GT grew rapidly in the mid-1990s. In the latter period (post-2002), there was a relative decline in gene therapy patents, which is partially explained by the completion of the Human Genome Project.

(Insert Figure 1a about here)

[7] There are several advantages of using Derwent for the purpose of this study. First, given the truly global nature of the biopharmaceutical industry, Derwent provides worldwide coverage of patent grants issued to biopharmaceutical firms. Second, the database accounts for the fact that firms may seek patent protection for the same invention in multiple jurisdictions as well as possibly having subsequent revisions to the original patent. A single patent record in the database (labelled as a patent family) often combines multiple patents related to the same invention. Third, Derwent has developed a proprietary patent technology classification system that allows for more effective identification of patents based on the function or the application domain to which the invention corresponds.

*External Research Alliances:* We used the ReCap database to capture research alliances for MAbs and GT. These arrangements are identified in Recap as either "CoL" (Collaboration Agreement) and/or "JV" (joint ventures). They go beyond a simple market-based exchange of IP for money; they are based on firms sharing organizational and managerial resources. Since we are interested in research investments, we only considered those agreements that are identified in Recap as "discovery" based and not those that are formed for commercialization.[8] We used the technology field in Recap to distinguish between alliances that are specific to MAbs and those that are specific to GT. In the early 1990s, there were on average more research alliances for GT than for MAbs. This trend was later reversed. More recently, research alliances for both MAbs and GT have been growing (Figure 1b).

(Insert Figure 1b about here)

*External Research Contracts:* Research contracts entail agreements wherein the firm licenses an IP or contracts its research to an external organization (typically a biotechnology entrant or a university). Using Recap's agreement type, we included those partnerships with either licensing (ReCap code L) or research contracting (ReCap code R) but which do not have a collaborative arrangement. Common to these agreements is that the biopharmaceutical incumbents pursue technology sourcing but do not share costs or collaborate through dedicated project groups or legal entities. Research contracting was an important mode for incumbents to pursue both MAbs and GT. The total number of research contracts for MAbs and GT tracked

[8] We control for the incumbents' use of commercialization (non-research) alliances in our estimations. These alliances represent collaborative arrangements in which biopharmaceutical incumbents partner with biotechnology start-ups for commercializing the start-ups discoveries but not for pursuing joint research (Nicholls-Nixon & Woo, 2003).

each other very closely until about 2002, when there were significantly more research contracts for MAbs than for GT (Figure 1c).

(Insert Figure 1c about here)

*Technology Acquisitions:* Figure 1d shows the trends for the number of technology acquisitions by incumbents in the sample focusing on MAbs and GT. We include all acquisitions in which the acquisition was classified by Recap as either MAbs or GT specific acquisition, or if the acquired target (usually a small biotechnology firm) had applied for either GT or MAbs patents or had GT or MAbs products in development, reflecting that these firms have technological capabilities within the respective regimes. Technology acquisitions were rare in the 1980s but proliferated in the 1990s and 2000s. Throughout the period of study, the number of acquisitions for GT and MAbs tracked each other closely.

(Insert Figure 1d about here)

In summary, the observed pattern of investments by incumbents in both MAbs and GT suggests that incumbents were not only adaptive with respect to the emerging technological regimes but also that their investments were being channeled through internal research units as well as through research contracts, alliances and acquisitions.

## HYPOTHESES TESTING

### Variables

*Dependent Variable:* In the biopharmaceutical industry, drug development is a long, uncertain process that is initiated through investments in research aimed at understanding the root cause of a given disease or illness and identifying potential therapeutic solutions. The commercialization stage begins with the initiation of preclinical trials (often toxicology studies on animals), which are then followed by heavily regulated trials on humans. The

biopharmaceutical value chain from initial research to final approval of a therapy or a drug is illustrated in Figure 2. Because of the substantial costs associated with commercialization, firms are very selective in channeling their potential therapeutic solutions discovered during the research stage through to the commercialization stage (Rothaermel & Deeds, 2004; Hess & Rothaermel, 2011). Only about 2.5% of all drug candidates explored in the initial research stage enter the preclinical trials (Giovannetti & Morrison, 2000; Hess & Rothaermel, 2011).

(Insert Figure 2 about here)

Given that our theory operates at the nexus of research and commercialization, we focused on the initiation of preclinical trials to observe incumbents' commercialization attempts within a given technological regime. In our interviews, managers and scientists confirmed the initiation of preclinical trials as an important strategic decision regarding whether the research output should be commercialized. In addition to personnel commitments, each preclinical trial entails substantial financial commitments, ranging from 1 to 15 million dollars. A senior manager at large biopharmaceutical incumbent explained the importance of preclinical trials in the drug development process:

> "Preclinical trials are the gatekeeper between research and commercialization, as at the preclinical stage, decisions take place with scientific, clinical and commercial input."

We used Pharmaprojects to identify therapeutic solutions in preclinical stage for MAbs (categorized within Pharmaproject biotech classification T3) and for GT (within Pharmaprojects biotech classification T4). For each preclinical entry, in order to ensure the year for initiating the preclinical stage was accurate, two researchers independently coded the information from Pharmaprojects. Further, we used a second database, Adis R&D Insights, to verify the year in

which the preclinical trial was initiated and to fill some of the missing data.[9] We used the earliest reported year in cases when the databases differed. The dependent variable, *Commercialization,* takes the value of 1 if we observe a new preclinical trial initiated by the incumbent firm for MAbs or GT in a given year, and 0 otherwise.[10]

*Independent Variables:* Given the complexity and uncertainty associated with the drug discovery process, it may take firms several years to translate their research investments into commercialization. In our interviews, scientists who are currently conducting and/or preparing for preclinical trials indicated that it takes between two and five years for a research project to reach the preclinical stage. This timeline for research is consistent with the existing literature on drug development (Rydzewski, 2008; Koehn & Carter, 2009). In our main analysis, we used a three-year window to measure firms' research investments, i.e., for the commercialization in year t, we observe incumbents' investments in the years t-1, t-2 and t-3 (e.g., Jiang, Tan, & Thursby, 2011). As additional robustness checks that we discuss after presenting our main results, we also used two- and four-year windows respectively. We measured firms' *internal research* investments using the count of patent grants applied for by the firm within a specific technological regime. The measures *research contracts*, *research alliances* and *technology acquisitions* are the number of research contracts, research alliances and technology acquisitions within a specific technological regime.

[9] Note that we use Adis R&D Insights as a supplementary database for validating information in our primary database, Pharmaprojects. Typically, the number of projects covered by Adis R&D Insights is lower than that covered by Pharmaprojects.

[10] For more than 90% of the observation years, incumbents initiated either one or no preclinical trials for GT and MAbs; for about 5% of the observation years, incumbents initiated two preclinical trials; for the remaining observation years, incumbents initiated 3-6 trials. Hence, the dependent variable does not have a strong correspondence with either the Poisson or the negative binomial distributions that are typically associated with the count data. Since most of the observations takes a value of zero and one, a binary outcome model provides a better fit to the data (Cameron & Trivedi, 2013). As an additional robustness check, we used the count of preclinical trials as the dependent variable and estimated a fixed effects negative binomial model. The results were qualitatively similar to our main results.

*Controls:* We controlled for a number of firm-level factors that may affect the likelihood of commercializing GT- or MAbs-based therapeutic solutions. We included the variable return on assets (*RoA),* which captures the firm's performance and may drive investments in the commercialization of emerging technological regimes (Greve, 1998). We included firm's *Total Assets* as a proxy for the firm's size as large firms may have more resources and greater access to complementary assets. *R&D intensity* (total R&D expenditures divided by total sales) provides a control for a firm's absorptive capacity (Cohen and Levinthal, 1990). We included *Total Pipeline* as the count of current products in FDA clinical trials, which is often considered an important indicator for the firm's drug development pipeline (Girotra, Terwiesch, & Ulrich, 2007). We also controlled for the overall commitments firms have within the specific technological regimes by including the total count of projects undergoing commercialization (preclinical and FDA trials) in a given year (*Projects in Development)* for both MAbs and GT. Given that firms may react to setbacks in a given technological regime (Greve, 1998), we also included a dichotomous variable, *Failure,* which takes a value of 1 if the firm discontinued a MAbs or GT project in clinical trials within the last three years and 0 otherwise. We included the variable *Non-research partnerships,* which reflects the exploitative orientation of the firm with respect to either GT or MAbs (e.g., Rothaermel, 2001). This was operationalized by the number of commercialization-oriented contracts and alliances within a three year period.

Pharmaceutical incumbents' pursuit of new biology-based technologies may be constrained by their existing chemical-based competencies (Leonard-Barton, 1992). We controlled for this effect by using the variable, *chemistry focus,* which is the ratio of firms'

chemistry-based patents vs. biotechnology patents.[11] The incumbents' pursuit of new biology-based technologies may also be affected by the cognition of the top managers (Kaplan, 2008). In order to control for this effect, we examined the CEO and/or Chairman's letters to shareholders in the annual reports. The measure, *cognition biotech*, is the count of biotechnology-related keywords that appear in the letter to shareholders by a firm in a given year (c.f. Kaplan, Murray, & Henderson, 2003).[12] All of the control variables are lagged by one year.

**Model**

We modeled the firm's likelihood of commercialization using a logistic specification. We used firm-level panel data to estimate the effects of firms' research investments on commercialization within each technology regime. This approach takes into account that unexplained variance across technological regimes may not be equal; however, it makes it more difficult to statistically compare differences in the coefficients between the two technological regimes (Allison, 1999). Statistical inferences can only be drawn if coefficients are significant in one regime but not in the other or by comparing the ratio of coefficients for two covariates across regimes (Train, 1998; Hoetker, 2007).[13] To control for unobserved firm-level heterogeneity and unobserved changes within a technological regime over time, we included firm and year fixed effects in our analysis (estimations are performed using STATA 11 "xtlogit, fe" conditional fixed

[11] We used Pharmaprojects patent data and linked it to Derwent to capture which Derwent Manual Codes are deployed by chemistry-based and biotechnology-based patents. The manual codes can be downloaded here: https://www.dropbox.com/s/0l8o39fe9f94jh0/Pharmaprojects_Patent_Derwent_MC.xlsx

[12] Keywords used: biotech, biologics, cloning, gene, genome, genomics, growth factor, molecular biology, monoclonal antibody, nucleotide, protein, DNA (or rDNA), gene therapy, antisense

[13] As an alternative, we could test Hypotheses 1 and 2 by interacting internal research and research contracts with a dummy variable that takes a value of 0 for MAbs and 1 for GT. However, this approach assumes that the unexplained variance is the same across the different technological regimes (Allison, 1999); violation of this assumption can lead to false inferences regarding the differences between the regimes (Hoetker, 2007). We used the test developed by Allison (1999) to confirm that the unobserved variation differs across MAbs and GT. Hence, we tested Hypotheses 1 and 2 by estimating separate models for MAbs and GT.

effects model procedure with year dummies).[14] The fixed effects estimation led to the omission of five firms that did not pursue the commercialization of both GT and MAbs during the period of study. The final analysis is based on 591 firm-year observations for MAbs and 561 firm-year observations for GT from a total of 45 incumbent firms.[15]

**Results**

Table 1 provides the descriptive statistics and Table 2, the bivariate correlation matrix for both MAbs and GT samples. Multicollinearity is not a concern. The mean variance inflation factor (VIF) for the final models was below 2.93 (MAbs) and 2.21 (GT). Individual VIFs for the independent variables were below 4.1 (MAbs) and 2.2 (GT), all well below the recommended cutoff levels of 10 (Neter, Wasserman, & Kutner, 1996) .

(Insert Tables 1 and 2 about here)

The estimates from the regression analysis are tabulated in Table 3. Models 1 and 2 are baseline models with control variables for MAbs and GT respectively. In both models, *failure* within the respective technological regime reduces the likelihood of commercialization. We further found that the *size* of the firm (total assets) and current *projects in development* within a technology regime increase the likelihood of commercialization for MAbs but not for GT. *Chemistry focus* decreases the likelihood of commercialization for both MAbs and GT but is only significant for GT.

[14] To check for autocorrelation in our dataset, we performed the Wooldridge's test (2002). The test could not reject the null hypothesis of no first-order autocorrelation.

[15] Among the 45 firms, 12 firms merged during the period of study. Moreover, 9 incumbents did not initiate any preclinical trial in GT and 6 incumbents did not initiate any preclinical trial in MAbs. These firms were dropped from the fixed effects analysis for the specific technological regimes. We ran additional robustness checks including the firms that did not initiate any preclinical trial in GT and/or MAbs using a random effects specification, and only including those firms that initiated the preclinical trials for both GT and MAbs using the fixed effects specification. The pattern of coefficients was very similar to the main results.

In Hypothesis 1, we predicted that the impact of incumbents' internal research on commercialization would be greater for MAbs than for GT. In order to test this hypothesis, we included the covariate *internal research* in Models 3 and 4. Consistent with our prediction, the coefficient for *internal research* is positive and significant for MAbs but not significant for GT. The difference between the coefficients is statistically significant ($p < 0.01$) using a Wald chi-square test (Allison, 1999). However, this test assumes that all other coefficients across the two models are equal. A less restrictive test is based on comparing the ratio of coefficients across the two models (Train, 1998; Hoetker, 2005, 2006). This requires a common covariate which is significant and similar in magnitude in both models as a denominator. The coefficient for *failure* within both technology regimes is negative and very similar in magnitude (-0.838 for MAbs and -1.061 for GT). The ratio of coefficients for *internal research* and *failure* is -0.090 for MAbs and is -0.006 for GT. Although statistical significance in the tests of differences between ratios of coefficients can be difficult to achieve (Hoetker, 2007), we find that the difference between the ratios is statistically significant ($p < 0.05$), offering support for Hypothesis 1.

Our arguments underlying Hypothesis 1 were also validated in our interviews. For example, a senior scientist in one of the top biopharmaceutical firms discussed the general challenges of commercializing in-house research:

> "Big pharma typically is run by managers not scientists – they have unique challenges. You know some companies – they do not want to make a drug out of it unless it makes 1billion dollar so basically commercial people will decide if it [research discovery] goes the next step or not."

When asked specifically about the difference between MAbs and GT, two senior business development executives at incumbent firms expressed their skepticism about GT and commented on greater business scrutiny for in-house GT-based research:

> "Compared to monoclonal antibodies…Gene Therapy is driven by personal health and niche applications…for a small set of patients you will command a very high price…the business case [for GT] is hard to establish."

> "The idea that in Gene Therapy, the technology in-house struggles to move forward in commercialization is not surprising…because again – this is the square peg round hole. We have it – does not look like an antibody, does not look like a small molecule – we are struggling [to justify the economic opportunity]"

Hence, both quantitative and qualitative evidence seem to support our conjecture that the commercialization of in-house research in GT was constrained due to its lack of fit with the incumbents' prevailing business model.

We tested Hypothesis 2 by including *research contracts* in Models 5 and 6. The coefficient for *research contracts* is positive and significant for MAbs but not for GT. The difference between the coefficients is statistically significant ($p < 0.01$) using the Wald test (Allison, 1999). The ratio of coefficients for *research contracts* and *failure* is -0.633 for MAbs and is -0.096 for GT. The difference between ratio of coefficients is statistically significant ($p < 0.05$), offering support for Hypothesis 2 that incumbents' investments through research contracts more likely lead to commercialization when the technological regime is sustaining than when it is disruptive. Therefore, while incumbents accessed external sources of knowledge underlying disruptive technologies through investments in contract research, the commercialization of such knowledge still seems to be subject to organizational inertia, as was the case with in-house research. In our interviews, a managing director highlighted the similarities in the commercialization decisions between in-house research and internal research:

> "Contract research and in-house research are both managed by the organization so there is no real difference regarding the commercialization decisions."

The commercialization of contract research was also subject to additional economic considerations because of royalty payments and the IP ownership by the contracting research

organization. This concern was voiced by a senior executive responsible for managing research contracts and partnerships involving incumbents:

> "With contract research, big Pharma firms are even more concerned about IP issues and royalty payments which raises the bar for the business justification."

In Models 7 and 8, we included the variable *research alliances* and in Models 9 and 10, we included the variable *technology acquisition*. Models 11 and 12 are fully specified models with all covariates. The coefficient estimate for research alliances is positive and significant for both MAbs and GT. The coefficient estimate for technology acquisitions is positive for both Mabs and GT but only significant for GT. We elaborate on this somewhat surprising insignificant effect of acquisition for MAbs in the discussion section. In Hypothesis 3, we predicted that when pursuing disruptive technological regimes, incumbents' investments in research alliances will more likely lead to commercialization than investments in internal research (H3a) or research contracts (H3b). It is possible that investments through research alliances may systematically be more likely to result in commercialization than investments through research contracts or internal research. Hence, simply testing the difference between coefficients for research alliances and research contracts (or internal research) for GT may create false inferences. A more reliable comparison can be drawn by comparing the ratio of coefficients for research alliances and research contracts (or internal research) between GT and MAbs in Models 11 and 12. The coefficient estimates for MAbs represent a control group for the relative impact of different types of investments on commercialization.

The coefficient for external research alliances is 0.473 for MAbs and is 0.641 for GT. The coefficient for *internal research* is 0.063 for MAbs and is 0.001 for GT. There is almost a hundred fold increase in the ratio of coefficients from MAbs (7.5) to GT (641). The difference between ratios is statistically significant ($p < 0.05$), supporting Hypothesis 2a. The ratio of

*research alliances* to *research contracts* was greater for GT (5.211) than for MAbs (0.918) and this difference was statistically significant ($p < 0.1$), supporting Hypothesis 3b.

Why is it that within a disruptive technological regime, investments through research alliances are more likely to lead to the initiation of commercialization than investments in contract and internal research? Our interviewees offered several insights that shed light on this interesting finding. For example, a business manager commented on the difference between external relationships created through research contracts and those created through research alliances:

> "Collaboration in research has an external partner whereas contract research has an external contractor. This is a major difference regarding who drives the research agenda and how critical decisions regarding the research are being made."

Many of the managers in incumbent biopharmaceutical firms discussed at length why alliances offered an organizational context that is separate from their internal organization and in which decisions and risks were jointly shared by their firms and the partners (start-ups or universities). For example, an interviewee commented that:

> "To add the biology expertise [from research partners], you need to come up with joint governance model. I have never seen such deals without the mutual efforts of both us [the incumbent] and our partners."

We also learnt that incumbents' research partners have strong incentives to commercialize their research despite an unproven business model. For example, a head of strategy of a large biopharmaceutical firm stressed that:

> "[external research partners] have to push their research to survive as they do not have other chances compared to a large pharma firm pursuing many projects at once."

Finally, an executive discussed the merit of research alliances to develop disruptive innovations:

> "Disruptive innovations are better managed through collaboration between big pharma companies and universities or start-ups because of sharing of risks and knowledge as well as collective decision making."

In Hypothesis 4, we predicted that relative to investments in internal research (H4a) or research contracts (H4b), those in technology acquisitions would have a greater effect on the likelihood of commercialization in disruptive technological regimes. Again, we use the sustaining technology regime as a reference group. The ratio of *technology acquisition* to *internal research* was much lower for MAbs (5) than for GT (1048). We tested the difference between ratios and found the difference to be statistically significant ($p < 0.01$), supporting Hypothesis 3a. Similarly, the ratio of *technology acquisition* to *research contracts* was greater for GT (6.82) than for MAbs (1.64) and this difference was statistically significant ($p < 0.05$), supporting Hypothesis 4b.

In our interviews, managers of biopharmaceutical incumbents offered several insights that are consistent with our arguments and help explain the effectiveness of acquisitions for commercializing disruptive technologies. We learnt that acquirers work hard to retain and incentivize key employees of the acquired firms who, according to the head of strategy in one incumbent firm, "have the magic." Interviewees explained the continued involvement of scientists and managers of the start-ups in the strategic decision making and the virtues of structural separation of acquired biotechnology start-ups:

> "While firms get integrated, the acquirer always tries to retain and incentivize key scientists and decision makers of the acquired firm to be part of the decision-making as you cannot afford to lose them…A lot of thought is given into this [structural autonomy vs. integration]. We would love to incentivize them on their own…most of the things follow technical project lifetime. In a few years remaining you pretty much know [if they are successful as an autonomous unit]."

> "We try to build a very much hands-off approach as we want to learn from the acquired entities."

In a separate supplemental analysis, we explored the extent to which biopharmaceutical incumbents in our sample preserved the structural autonomy of acquired firms. We checked as to whether research papers published by scientists of acquired start-ups continued to have the name of their start-ups as the scientists' affiliated organizations at least three years after the acquisition. We found that 84% of these acquired firms were still being mentioned as the scientists' affiliated organizations. Hence, similar to Schweizer (2005), we found strong support for the premise that biopharmaceutical incumbents tend to preserve the structural autonomy of the acquired start-ups.

**Robustness Checks**

We conducted several additional checks to establish the robustness of our findings, which are shown in Table 4. First, instead of counts, we operationalized the independent variables as dichotomous variables that capture whether an incumbent invested in internal research, research contracts, research alliances and technology-based acquisitions (Models 13 and 14).[16] In our main results, we used a three year observational window for the independent variables. To ensure that our results were not sensitive to the choice of this window, we used windows of two and four years respectively (Models 15-18). Results in all these models are very similar to the ones reported in Models 11 and 12.

Despite using year fixed effects, it is possible that firms may pursue different strategies during different periods of the emergence of MAbs and GT. We identified three distinct periods in which such strategic change may have occurred. First, we observed a relative decline in the patenting and research contracting for GT after 2002. One concern could be that this decline

[16] Internal research takes a value of 1 if the incumbent firm had applied for at least five patent grants within a technological regime during a three year period, and 0 otherwise. The threshold of five patents was chosen to ensure that these investments are substantial and to reduce the likelihood of measurement error due to misclassified patents.

might be correlated with a systematic reduction in the incumbents' incentives towards commercializing GT. To address this concern, we limited our analysis to the pre-2003 period (Models 19 and 20). Separately, in order to ensure that our results were not impacted by unobserved differences in incumbents' strategies during the Human Genome project, we excluded the years 1998-2002 from the analysis (Model 21 and 22). We also limited our analysis to the post-1997 period to exclude the initial emergence period of the new technological regime as incumbents may be somewhat less likely to pursue commercialization during this nascent stage (Models 23 and 24). The estimates in these models (Models 19-24) confirm that the patterns we observed were not driven by a specific time period.

We conducted a number of additional robustness checks.[17] For some observations in our data set, firms did not invest in either MAbs or GT (i.e., the value of all of the independent variables was 0 for a given observational year). It is possible that these observations represent periods where firms may either have had no interest in these emerging technological regimes or may have changed their strategy. The results are robust to the exclusion of these observations from the analysis. To account for the possibility that some firms may focus their commercialization efforts in only one technological regime, we ran an analysis in which we excluded those firms that initiated the preclinical commercialization stage for only one of the two technological regimes during the study period. The results for the independent variables were almost identical to our main results. Finally, we used an instrumental variable approach to account for the potential endogeneity of firms' drawing on external sources of knowledge (i.e., contracting, alliances and acquisitions). We used three different instruments that are likely correlated with firms' choices to pursue research contracts, alliances and acquisitions within a given technological regime but uncorrelated with the firms' initiation of preclinical trials in that

[17] These results are available from the authors. They are not included because of space constraints.

regime. The first instrument is the total number of research contracts, alliances and acquisitions that a firm pursues within a three year period that are not targeted towards the specific technological regime. This is reflective of the firms' general openness to draw on external sources of knowledge that is not directly correlated with the initiation of the preclinical trial in either MAbs or GT. The other two instruments are the ratio of the number of alliances and acquisitions over the total number of externally oriented investments, and capture the preference of a firm to use a specific mode. We instrument each mode of investment separately. We ran tests to ensure that our instrumental variables were relevant and valid. The estimates using the instrumental variable analysis followed similar patterns to our main results. The results of these additional robustness checks gave us greater confidence concerning our analysis.

## DISCUSSION AND CONCLUSION

The innovation literature has long focused on the challenges that incumbents face in managing radical technological change. We contribute to this inquiry by exploring the relationship between incumbents' investments and commercialization of radical technological regimes. In so doing, we offer a framework that helps to explain when incumbents' well-intended investments are likely to yield successful adaptation and when they may be voided by the forces of inertia.

We consider the possibility that, beyond supply-side competence destruction, radical technological regimes may also lack the demand-side fit with the incumbents' prevailing business model (Abernathy & Clark, 1985; Christensen & Raynor, 2003). We argue that this is an important but underexplored source of organizational rigidity associated with the incumbent's commercialization of new technologies. We further consider the different ways in which incumbents may choose to pursue radical technologies. These include the often emphasized

investments in their internal research units but also investments channelled towards entrants and research organizations through the use of research contracts, research alliances and acquisitions (e.g., Nicholls-Nixon & Woo, 2003). These modes differ in the extent to which the exploration of the new technology is structurally separated from the incumbents' incentive structures, organizational routines, and resource allocation processes, and involves outside influence on strategic decision making. This helps to explain why incumbents, despite investing in radical technologies and having access to complementary assets, may still be unable to manage technological change, and what types of investments will be more effective in overcoming organizational rigidity and achieving desired commercialization outcomes.

The context for the study is the global biopharmaceutical industry, which recently witnessed the emergence of two revolutionary therapeutic approaches based on genetic engineering – MAbs and GT. While MAbs and GT drew on incumbents' specialized complementary assets, they differed in their fit with the incumbents' business model. MAbs matched the existing business model of incumbent firms (i.e., long term treatment often administered at home, resulting in yearly treatment costs for patients and insurers); GT was much more disruptive (i.e., typically one-off or significantly less frequent treatment administered by the physicians). Incumbents responded to these emerging technologies by undertaking internal research investments as well as drawing on external sources of knowledge through the use of research contracts, alliances and acquisitions. However, the extent to which these investments resulted in commercialization differed between MAbs and GT. Investments in internal research and contract research led to the commercialization for MAbs (the sustaining technological regime) but not for GT (the disruptive technological regime). This is evidence that the commercialization of knowledge developed in-house or accessed through contract research is

subject to organizational rigidity if the technological regime is disruptive. In contrast to investments in internal and contract research, those in research alliances and acquisitions had a significant effect on the commercialization for GT. Hence, research alliances and acquisitions seem to offer an organizational context that is shielded from incumbents' inertial pressures stemming from disruptive technologies.

In our interviews, industry participants offered several insights that provided additional support for our arguments and findings. We learnt why, as compared to research investments in MAbs, those in GT were subject to greater skepticism and scrutiny by strategic decision makers within the incumbent organization. We also learnt that while incumbents may undertake investments in contract research in order to access new knowledge beyond their boundaries, the organizational processes underlying commercialization are no different from those involving investments in internal research. Hence, incumbents' investments in contract research toward GT tended to suffer from similar commercialization challenges to those in internal research. Finally, we were able to uncover why, in contrast to investments in internal and contract research, those in alliances and acquisitions had a significant impact on the commercialization for GT. Both alliances and acquisitions represented investments that were structurally separated from the parent organization and involved outsiders (typically scientists and managers from start-ups) in the decision-making processes. This created an organizational context which motivated the pursuit of opportunities within GT, and which was isolated from the demands and constraints associated with the incumbents' prevailing business models.

Taken together, these findings illustrate that our understanding of how technological change impacts firms is incomplete without an explicit consideration of how the change interacts with the incumbents' business model and what organizational modes are used by incumbents to

access and develop new knowledge. Hence, we are able to offer a new set of organizational and strategic contingencies to the question of how technological change impacts firms.

The study also sheds light on a frequent misconception regarding disruptive technologies that incumbents fail to invest in such technologies. As documented in several case studies, incumbents often do invest in such technologies (Christensen & Bower, 1996; Sull et al., 1997; Tripsas & Gavetti, 2000; Gilbert, 2005). However, as our results illustrate, many of the initial research investments in disruptive technologies may not lead to subsequent commercialization. This suggests that the locus of incumbent inertia is not necessarily at the point of investment but rather at the point of commercialization. Investments channeled towards technology start-ups and research organizations through collaborative alliances and acquisitions may offer incumbents with a means to overcome that inertia.

Further, the difference in the impact between investments in research contracts and those in research alliances offers an important distinction between incumbents' actions and decisions during periods of technological change. While incumbents may act to draw on knowledge of entrants and research organizations through research contracts and alliances, these arrangements vary in the extent to which the decisions for commercialization are externalized. The locus of decision making remains internal in the case of unilateral market-based research contracts while extending outwards in the case of bilateral research alliances. As we learnt during our interviews, this is an important difference regarding which investments are more likely to yield commercialization of disruptive technologies.

Finally, by disaggregating the biotechnology field into specific technological regimes, we are also able to shed light on the somewhat unexpected findings of earlier studies (Rothaermel, 2001; Nicholls-Nixon & Woo, 2003). For example, despite arguing that pharmaceutical firms'

upstream investments in biotechnology would result in greater levels of product commercialization, Nicholls-Nixon and Woo did not find a significant relationship between the different types of research investments and commercialization. Our findings suggest that this could be a result of aggregating distinct technological regimes, which may interact very differently with the incumbents' organizational and strategic context.

The study has a number of limitations, which should provide ample opportunities for future research. First, it was conducted in the context of a single industry and the generalizability of our findings and their boundary conditions would need to be validated through explorations in other empirical contexts. Second, while our focus on MAbs and GT provided us with a unique opportunity to study two distinct types of technological regimes that emerged around the same time in the biopharmaceutical industry, the newness of these regimes and the long commercialization cycles in the industry did not allow us to observe the final commercialization outcomes (product approval and market share). Consistent with our theory that operates at the nexus of invention (generation of new knowledge) and innovation (commercialization of new knowledge), we observed the initiation of commercialization through preclinical trials. Industry participants confirmed the decision to initiate preclinical trials as an important strategic decision that incumbents make in commercializing newly discovered therapeutic solutions. However, we are unable to draw inferences regarding final commercialization outcomes such as product sales or firms' profits (e.g., Polidoro & Toh, 2011). Third, ideally, we would have preferred to observe the commercialization outcomes for each research project that biopharmaceutical incumbents pursued for MAbs and GT. However, such archival data for early stage research projects are not publicly available. While our approach is consistent with prior studies (Nicholls-Nixon & Woo, 2003; Hess & Rothaermel, 2011), it would be valuable to undertake in-depth

explorations of specific research projects that incumbents pursue through a variety of organizational modes. Finally, while we performed a number of robustness checks with respect to model estimations and the operationalization of variables, we were unable to fully resolve issues related to potential measurement errors. For example, while we are able to draw on established categorization schema with respect to MAbs and GT to identify incumbents' investments in internal research, research contracting and research alliances, we were somewhat limited in our ability to precisely identify acquisitions as pertaining to MAbs and GT. Some acquired targets were startups that pursued both the technological regimes and hence, our inferences with respect to acquisitions as a means to invest in a specific technological regime may not hold. This may explain the somewhat unexpected statistically insignificant effect of acquisitions on the commercialization for MAbs, and may be an opportunity for future research to more fully explore the role of acquisitions during periods of technological change.

Despite these and other limitations, we hope that the study offers an important contribution to our understanding of how technological change impacts firms. While incumbents often respond to and invest in new technologies, we show that their commercialization efforts may still be subject to organizational constraints stemming from inconsistencies with respect to their business models. In contrast to investments in internal and contract research, those in research alliances and acquisitions offer a means to overcome such inertial forces and help incumbents navigate the changing technology landscape. In so doing, we contribute to the theoretical agenda of moving beyond "adaptability vs. rigidity" to developing a richer understanding of the ways in which these elements interact and shape the behavior of firms in the face of technological change.

## BIBLIOGRPAHY


Abernathy, W. J., & Clark, K. B. 1985. Innovation - Mapping the winds of creative destruction. ***Research Policy***, 14(1): 3-22.

Adegbesan, J. A., & Higgins, M. J. 2011. The intra-alliance division of value created through collaboration. ***Strategic Management Journal***, 32(2): 187-211.

Adner, R., & Levinthal, D. 2008. Doing versus seeing: acts of exploitation and observations of exploration. ***Strategic Entrepreneurship Journal***, 2(1): 43-52.

Allison, P. D. 1999. Comparing logit and probit coefficients across groups. ***Sociological Methods & Research***, 28(2): 186-208.

Anand, J., Oriani, R., & Vassolo, R. S. 2010. Alliance Activity as a Dynamic Capability in the Face of a Discontinuous Technological Change. ***Organization Science***, 21(6): 1213-1232.

Anderson, P., & Tushman, M. L. 1990. Technological discontinuities and dominant designs: a cyclical model of technological change. ***Administrative Science Quarterly***, 35(4): 604-633.

Arora, A., Fosfuri, A., & Gambardella, A. 2001. ***Markets for technology: The economics of innovation and corporate strategy***. Cambridge: MIT Press.

Burgelman, R. 1983. Corporate entrepreneurship and strategic management: Insights from a process study. ***Management Science***, 29(12): 1349-1364.

Burgelman, R. A., & Grove, A. S. 1996. Strategie Dissonance. ***California Management Review***, 38(2).

Burns, L. R. 2005. ***The business of healthcare innovation***: Cambridge Univ Press.

Cameron, A., & Trivedi, P. 2013. ***Regression analysis of count data***: Cambridge University Press.

Chaudhuri, S., & Tabrizi, B. 1999. Capturing the real value in high-tech acquisitions. ***Harvard Business Review***, 77(5): 123.

Chesbrough, H. 2001. ***Assembling the elephant: a review of empirical studies on the impact of technical change upon incumbent firms***: Emerald Group Publishing Limited.

Christensen, C. M. 1997. ***The innovator's dilemma: when new technologies cause great firms to fail***. Boston, MA: Harvard Business School Press.

Christensen, C. M. 2006. The Ongoing Process of Building a Theory of Disruption. ***Journal of Product Innovation Management***, 23(1): 39-55.

Christensen, C. M., & Bower, J. L. 1996. Customer power, strategic investment, and the failure of leading firms. ***Strategic Management Journal***, 17(3): 197-218.

Christensen, C. M., & Raynor, M. 2003. ***The innovator's solution***: Harvard Business School Press Boston.

Christensen, C. M., & Rosenbloom, R. S. 1995. Explaining the attacker's advantage: technological paradigms, organizational dynamics, and the value network. ***Research Policy***, 24: 233-257.

Cooper, A. C., & Schendel, D. 1976. Strategic responses to technological threats. ***Business Horizons***, 19(1): 61-69.

Creswell, J. W., & Clark, V. L. P. 2011. ***Designing and conducting mixed methods research***: Wiley Online Library.

Dosi, G. 1982. Technological paradigms and technological trajectories. ***Research Policy***, 11: 147-162.

Dubois, S. 2012. 5 science breakthroughs in 2012, ***Fortune***.

Eggers, J. P., & Kaplan, S. 2009. Cognition and renewal: Comparing CEO and organizational effects on incumbent adaptation to technical change. ***Organization Science***, 20(2): 461-477.

Foster, R. N. 1986. ***Innovation: The attacker's advantage***: Summit Books New York.

Freeman, C., & Soete, L. 1997. ***The economics of industrial innovation*** (3rd ed. ed.): Pinter Press, London, UK.

Furr, N. R., Cavarretta, F., & Garg, S. 2012. Who changes course? The role of domain knowledge and novel framing in making technology changes. ***Strategic Entrepreneurship Journal***, 6(3): 236-256.

Gambardella, A. 1992. Competitive advantages from in-house scientific research: the US pharmaceutical industry in the 1980s. ***Research Policy***, 21(5): 391-407.

Gilbert, C. G. 2005. Unbundling the Structure of Inertia: Resource versus Routine Rigidity. ***Academy of Management Journal***: 741-763.
Giovannetti, G., & Morrison, S. 2000. Convergence. The biotechnology industry report. ***Ernst & Young***.
Girotra, K., Terwiesch, C., & Ulrich, K. T. 2007. Valuing R&D projects in a portfolio: Evidence from the pharmaceutical industry. ***Management Science***, 53(9): 1452-1466.
Graebner, M. E., Eisenhardt, K. M., & Roundy, P. T. 2010. Success and failure in technology acquisitions: Lessons for buyers and sellers. ***Academy of Management Perspectives***, 24(3): 73-92.
Greve, H. 1998. Performance, Aspirations, and Risky Organizational Change. ***Administrative Science Quarterly***, 43(1).
Gulati, R., & Singh, H. 1998. The Architecture of Cooperation: Managing Coordination Costs and Appropriation Concerns in Strategic Alliances. ***Administrative Science Quarterly***, 43(4): 781-814.
Henderson, R. 1993. Underinvestment and incompetence as responses to radical innovation: Evidence from the photolithographic alignment equipment industry. ***The RAND Journal of Economics***: 248-270.
Henderson, R., & Clark, K. B. 1990. Architectural innovation: the reconfiguration of existing product technologies and the failures of established firms. ***Administrative Science Quarterly***, 35(1): 9-30.
Hess, A., & Rothaermel, F. 2011. When are assets complementary? Star scientists, strategic alliances, and innovation in the pharmaceutical industry. ***Strategic Management Journal***, 32(8): 895-909.
Hill, C., & Rothaermel, F. 2003. The performance of incumbent firms in the face of radical technological innovation. ***Academy of Management Review***, 28(2): 257-274.
Hoetker, G. 2005. How much you know versus how well I know you: selecting a supplier for a technically innovative component. ***Strategic Management Journal***, 26(1): 75-96.
Hoetker, G. 2006. Do modular products lead to modular organizations? ***Strategic Management Journal***, 27(6): 501-518.
Hoetker, G. 2007. The use of logit and probit models in strategic management research: critical issues. ***Strategic Management Journal***, 28(4): 331-343.
Jiang, L., Tan, J., & Thursby, M. 2011. Incumbent firm invention in emerging fields: evidence from the semiconductor industry. ***Strategic Management Journal***, 32(1): 55-75.
Kale, P., & Singh, H. 2009. Managing Strategic Alliances: What Do We Know Now, and Where Do We Go From Here? ***The Academy of Management Perspectives***, 23(3): 45-62.
Kaplan, S. 2008. Cognition, capabilities, and incentives: assessing firm response to the fiber-optic revolution. ***Academy of Management Journal***, 51(4): 672-695.
Kaplan, S., & Henderson, R. 2005. Inertia and incentives: Bridging organizational economics and organizational theory. ***Organization Science***, 16(5): 509-521.
Kaplan, S., Murray, F., & Henderson, R. 2003. Discontinuities and senior management: Assessing the role of recognition in pharmaceutical firm response to biotechnology. ***Industrial and Corporate Change***, 12(2): 203-233.
Kaplan, S., & Tripsas, M. 2008. Thinking about technology: Applying a cognitive lens to technical change. ***Research Policy***, 37(5): 790-805.
Koehn, F. E., & Carter, G. T. 2009. Rediscovering natural products as a source of new drugs. ***Discovery Medicine***, 5(26): 159-164.
Leonard-Barton, D. 1992. Core capabilities and core rigidities: A paradox in managing new product development. ***Strategic Management Journal***, 13(1): 111-125.
Leone, M. I., & Reichstein, T. 2012. Licensing-in fosters rapid invention! the effect of the grant-back clause and technological unfamiliarity. ***Strategic Management Journal***, 33(8): 965-985.
Markman, G. D., Gianiodis, P. T., Phan, P. H., & Balkin, D. B. 2005. Innovation speed: Transferring university technology to market. ***Research Policy***, 34(7): 1058-1075.
Miller, D. W., & Feldman, S. R. 2006. Cost-effectiveness of moderate-to-severe psoriasis treatment.
Moran, N. 2012. First gene therapy approved. ***Nature Biotechnology***, 30(12): 1153-1153.

Nelson, R., & Winter, S. 1982. ***An evolutionary theory of economic change***. Cambridge, MA: Belknap Press.
Neter, J., Wasserman, W., & Kutner, M. H. 1996. ***Applied linear statistical models***: Irwin Chicago.
Nicholls-Nixon, C. L., & Woo, C. Y. 2003. Technology sourcing and output of established firms in a regime of encompassing technological change. ***Strategic Management Journal***, 24(7): 651-666.
Pisano, G. P. 1990. The R&D boundaries of the firm: An empirical analysis. ***Administrative Science Quarterly***, 35: 153-176.
Pisano, G. P. 2006. ***The science business: The promise, the reality, and the future of biotech***: Harvard Business Press.
Polidoro, F., & Toh, P. K. 2011. Letting Rivals Come Close or Warding Them Off? The Effects of Substitution Threat on Imitation Deterrence. ***Academy of Management Journal***, 54(2): 369-392.
Puranam, P., Singh, H., & Chaudhuri, S. 2009. Integrating acquired capabilities: When structural integration is (un) necessary. ***Organization Science***, 20(2): 313-328.
Puranam, P., Singh, H., & Zollo, M. 2003. A bird in the hand or two in the bush? Integration trade-offs in technology grafting acquisitions. ***European Management Journal***, 21(2): 179-184.
Ranft, A. L., & Lord, M. D. 2002. Acquiring new technologies and capabilities: a grounded model of acquisition implementation. ***Organization Science***, 13(4): 420-441.
Rosenbloom, R. S. 2000. Leadership, Capabilities, and Technological Change: The Transformation of NCR in the Electronic Era. ***Strategic Management Journal***, 21(10-11): 1083-1103.
Rothaermel, F., & Deeds, D. 2004. Exploration and exploitation alliances in biotechnology: A system of new product development. ***Strategic Management Journal***, 25(3): 201-221.
Rothaermel, F. T. 2001. Incumbent's advantage through exploiting complementary assets via interfirm cooperation. ***Strategic Management Journal***, 22(6-7): 687-699.
Rydzewski, R. M. 2008. ***Real world drug discovery: a chemist's guide to biotech and pharmaceutical research***: Elsevier Science.
Schilling, M. A. 2009. Understanding the Alliance Data. ***Strategic Management Journal***, 30(3): 233-260.
Schweizer, L. 2005. Organizational Integration of Acquired Biotechnology Companies into Pharmaceutical Companies: The Need for a Hybrid Approach. ***Academy of Management Journal***: 1051-1074.
Sosa, M. L. 2012. Organizational Structure, Real Options and the Advantage of De Novo Firms. ***London Business School working paper***.
Steensma, H. K., & Corley, K. G. 2000. On the performance of technology-sourcing partnerships: the interaction between partner interdependence and technology attributes. ***Academy of Management Journal***: 1045-1067.
Sull, D. N., Tedlow, R. S., & Rosenbloom, R. S. 1997. Managerial commitments and technological change in the US tire industry. ***Industrial and Corporate Change***, 6(2): 461-500.
Train, K. E. 1998. Recreation demand models with taste differences over people. ***Land economics***: 230-239.
Tripsas, M. 1997. Unraveling the process of creative destruction: complementary assets and incumbent survival in the typesetter industry. ***Strategic Management Journal***, 18(Summer Special Issue): 119-142.
Tripsas, M., & Gavetti, G. 2000. Capabilities, cognition and inertia: evidence from digital imaging. ***Strategic Management Journal***, 21: 1147-1161.
Tushman, M. L., & Anderson, P. 1986. Technological discontinuities and organizational environments. ***Administrative Science Quarterly***, 31(3): 436-465.
Utterback, J. M. 1994. Mastering the Dynamics of Innovation: How Companies Can Seize Opportunities in the Face of Technological Change Harvard Business School Press. ***Boston, MA***.
Wilson, J. M. 2012. It's time for gene therapy to get disruptive! ***Human Gene Therapy***, 23(1): 1.
Wooldridge, J. M. 2002. ***Econometric analysis of cross section and panel data***. Cambridge, Massachusetts: The MIT Press.
Wu, B., Wan, Z., & Levinthal, D. 2013. Complementary Assets as Pipes and Prisms: Innovation Incentives and Trajectory Choices. ***Strategic Management Journal***, forthcoming.

**Figure 1: Trends in Incumbents Research Investments towards Monoclonal Antibodies (MAbs) and Gene Therapy (GT)**

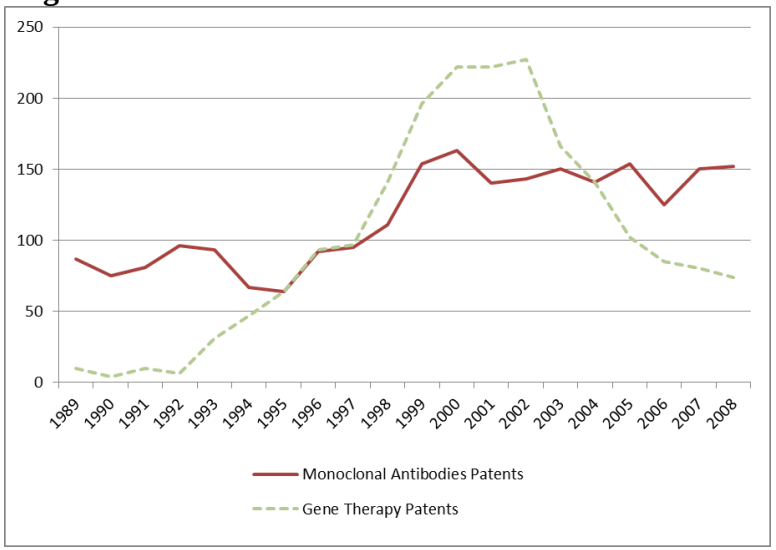


Figure 1a: Total Patents

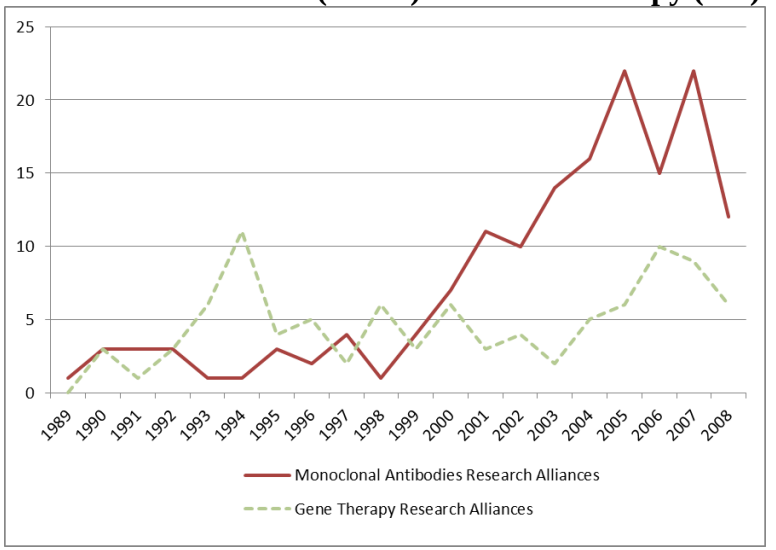


Figure 1b: Total Research Alliances

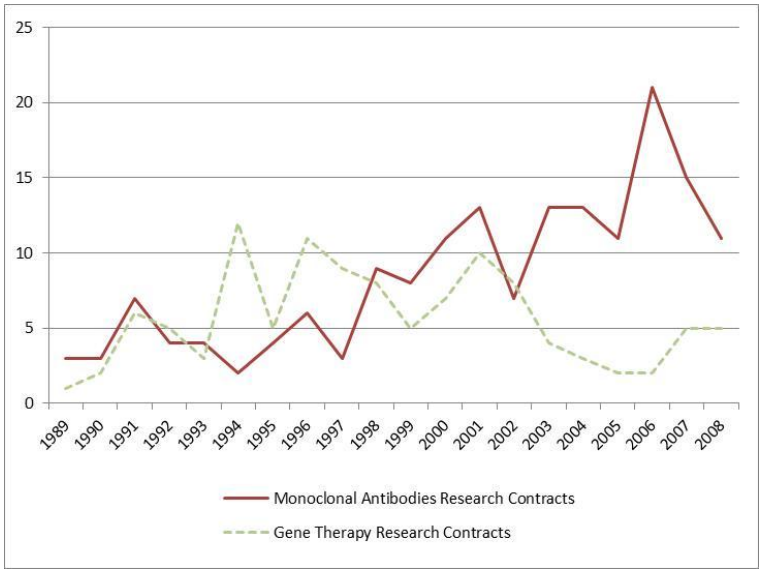


Figure 1c: Total Research Contracts

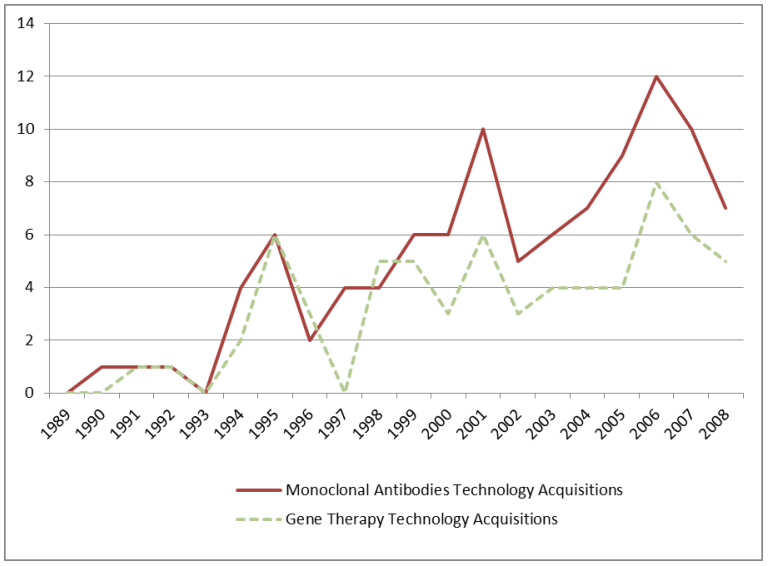


Figure 1d: Total Acquisitions

**Figure 2: Biopharmaceutical Industry's Innovation Value Chain**

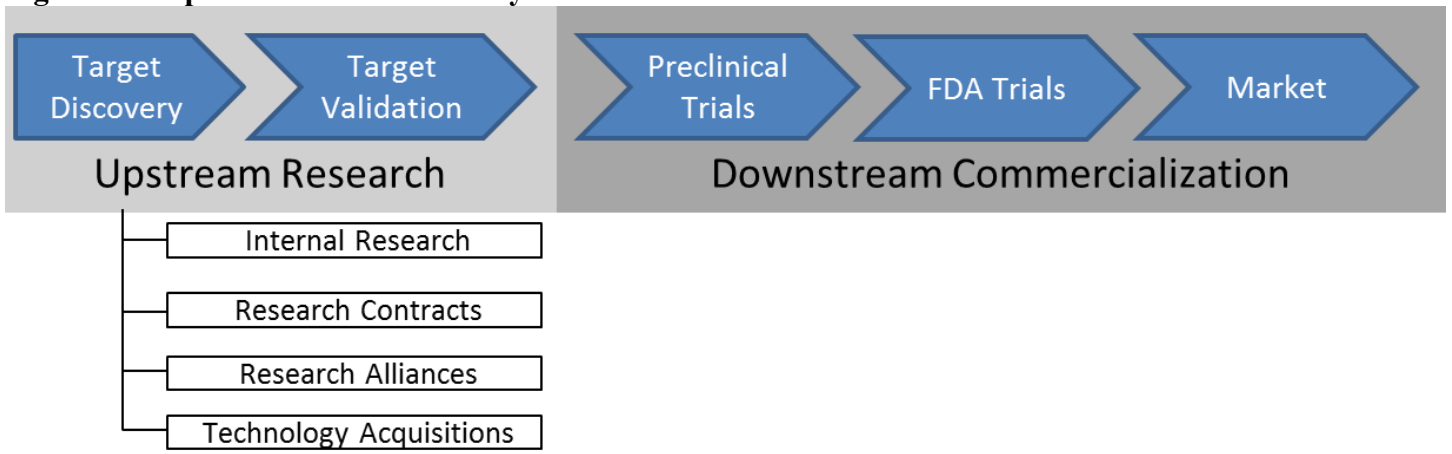


**Table 1 Descriptive Statistics**

| Monoclonal Antibody (n=591) | mean | sd | min | max |
|---|---|---|---|---|
| Commercialization | 0.29 | 0.45 | 0.00 | 1.00 |
| R&D Intensity | 0.13 | 0.07 | 0.03 | 0.74 |
| Projects in Development | 3.94 | 5.33 | 0.00 | 19.00 |
| Total Assets (log) | 9.21 | 1.10 | 5.91 | 11.84 |
| Financial Slack | 2.17 | 0.97 | 1.01 | 4.46 |
| RoA | 0.13 | 0.08 | -0.20 | 0.41 |
| Total Pipeline (PI-III) | 12.02 | 9.73 | 0.00 | 41.00 |
| Chemistry Preference | 0.57 | 0.19 | 0.00 | 1.00 |
| Failure | 0.19 | 0.38 | 0.00 | 1.00 |
| Non Research Partnerships | 0.95 | 1.84 | 0.00 | 12.00 |
| Cognition Biotech. | 0.75 | 1.64 | 0.00 | 14.00 |
| Internal Research | 9.72 | 12.74 | 0.00 | 65.00 |
| Research Contracts | 0.53 | 1.02 | 0.00 | 6.00 |
| Research Alliances | 0.61 | 1.21 | 0.00 | 8.00 |
| Technology Acquisition | 0.26 | 0.63 | 0.00 | 5.00 |

| Gene Therapy (n=561) | mean | sd | min | max |
|---|---|---|---|---|
| Commercialization | 0.24 | 0.43 | 0.00 | 1.00 |
| R&D Intensity | 0.13 | 0.07 | 0.03 | 0.74 |
| Projects in Development | 1.74 | 2.87 | 0.00 | 14.00 |
| Total Assets (log) | 9.10 | 1.22 | 5.91 | 11.84 |
| Financial Slack | 2.17 | 0.97 | 1.01 | 4.46 |
| RoA | 0.12 | 0.08 | -0.20 | 0.41 |
| Total Pipeline (PI-III) | 11.59 | 9.68 | 0.00 | 40.00 |
| Chemistry Preference | 0.56 | 0.18 | 0.02 | 0.87 |
| Failure | 0.11 | 0.32 | 0.00 | 1.00 |
| Non Research Partnerships | 0.33 | 0.92 | 0.00 | 9.00 |
| Cognition Biotech. | 0.78 | 1.64 | 0.00 | 14.00 |
| Internal Research | 10.83 | 18.15 | 0.00 | 91.00 |
| Research Contracts | 0.26 | 0.52 | 0.00 | 3.00 |
| Research Alliance | 0.40 | 0.71 | 0.00 | 5.00 |
| Technology Acquisition | 0.22 | 0.59 | 0.00 | 5.00 |

**Table 2 Correlation Table** (values above/below 0.1/-0.1 indicates significance of p<0.01)

| | MAbs (n=591) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Commercialization | 1.00 | | | | | | | | | | | | | | |
| 2 | R&D Intensity | 0.20 | 1.00 | | | | | | | | | | | | | |
| 3 | Projects in Development | 0.42 | 0.28 | 1.00 | | | | | | | | | | | | |
| 4 | Financial Slack | 0.07 | 0.36 | -0.05 | 1.00 | | | | | | | | | | | |
| 5 | RoA | 0.13 | -0.03 | 0.10 | -0.17 | 1.00 | | | | | | | | | | |
| 6 | Total Assets (log) | 0.24 | -0.15 | 0.44 | -0.32 | 0.13 | 1.00 | | | | | | | | | |
| 7 | Total Pipeline (PI-III) | 0.19 | 0.08 | 0.27 | -0.08 | 0.19 | 0.40 | 1.00 | | | | | | | | |
| 8 | Chemistry Preference | -0.10 | -0.33 | -0.16 | -0.12 | 0.01 | 0.08 | 0.28 | 1.00 | | | | | | | |
| 9 | Failure | 0.12 | 0.07 | 0.44 | -0.12 | 0.02 | 0.25 | 0.29 | -0.09 | 1.00 | | | | | | |
| 10 | Non Research Partnerships | 0.29 | 0.26 | 0.62 | 0.02 | 0.05 | 0.23 | 0.20 | -0.19 | 0.33 | 1.00 | | | | | |
| 11 | Cognition Biotech. | 0.13 | 0.24 | 0.33 | 0.02 | 0.01 | 0.05 | -0.01 | -0.30 | 0.11 | 0.30 | 1.00 | | | | |
| 12 | Internal Research | 0.43 | 0.40 | 0.59 | 0.07 | 0.04 | 0.33 | 0.15 | -0.35 | 0.29 | 0.46 | 0.33 | 1.00 | | | |
| 13 | Research Contracts | 0.40 | 0.21 | 0.49 | -0.01 | 0.04 | 0.31 | 0.19 | -0.14 | 0.27 | 0.40 | 0.24 | 0.52 | 1.00 | | |
| 14 | Research Alliances | 0.43 | 0.25 | 0.55 | 0.00 | 0.10 | 0.38 | 0.18 | -0.12 | 0.25 | 0.44 | 0.27 | 0.53 | 0.51 | 1.00 | |
| 15 | Technology Acquisitions | 0.25 | 0.11 | 0.51 | -0.07 | 0.08 | 0.33 | 0.27 | -0.02 | 0.25 | 0.29 | 0.09 | 0.30 | 0.30 | 0.32 | 1.00 |

| | GT (n=561) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Commercialization | 1.00 | | | | | | | | | | | | | | |
| 2 | R&D Intensity | 0.01 | 1.00 | | | | | | | | | | | | | |
| 3 | Projects in Development | 0.41 | 0.10 | 1.00 | | | | | | | | | | | | |
| 4 | Financial Slack | -0.12 | 0.39 | -0.17 | 1.00 | | | | | | | | | | | |
| 5 | RoA | 0.08 | -0.05 | 0.07 | -0.18 | 1.00 | | | | | | | | | | |
| 6 | Total Assets (log) | 0.32 | -0.12 | 0.42 | -0.34 | 0.16 | 1.00 | | | | | | | | | |
| 7 | Total Pipeline (PI-III) | 0.29 | 0.06 | 0.36 | -0.12 | 0.21 | 0.47 | 1.00 | | | | | | | | |
| 8 | Chemistry Preference | -0.01 | -0.41 | -0.07 | -0.30 | 0.02 | 0.14 | 0.32 | 1.00 | | | | | | | |
| 9 | Failure | 0.12 | 0.01 | 0.55 | -0.11 | -0.13 | 0.24 | 0.06 | -0.15 | 1.00 | | | | | | |
| 10 | Non Research Partnerships | 0.31 | 0.10 | 0.46 | -0.15 | 0.05 | 0.32 | 0.29 | 0.07 | 0.11 | 1.00 | | | | | |
| 11 | Cognition Biotech. | 0.02 | 0.26 | -0.05 | 0.01 | -0.02 | 0.01 | -0.05 | -0.34 | 0.08 | 0.04 | 1.00 | | | | |
| 12 | Internal Research | 0.19 | 0.21 | 0.33 | 0.02 | -0.02 | 0.34 | 0.18 | -0.27 | 0.31 | 0.24 | 0.20 | 1.00 | | | |
| 13 | Research Contracts | 0.30 | 0.02 | 0.49 | -0.17 | -0.03 | 0.28 | 0.18 | -0.06 | 0.35 | 0.29 | 0.04 | 0.30 | 1.00 | | |
| 14 | Research Alliances | 0.38 | 0.08 | 0.47 | -0.13 | 0.05 | 0.24 | 0.23 | -0.05 | 0.27 | 0.28 | -0.04 | 0.21 | 0.53 | 1.00 | |
| 15 | Technology Acquisitions | 0.29 | 0.10 | 0.42 | -0.12 | 0.14 | 0.36 | 0.29 | -0.01 | 0.12 | 0.50 | 0.02 | 0.18 | 0.07 | 0.21 | 1.00 |

**Table 3: Conditional Fixed Effects Logit Estimates for Incumbents' Commercialization**

| | (1) MAbs | (2) GT | (3) MAbs | (4) GT | (5) MAbs | (6) GT | (7) MAbs | (8) GT | (9) MAbs | (10) GT | (11) GT | (12) GT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R&D Intensity | -1.947 | -2.393 | -2.171 | -2.174 | -1.100 | -2.329 | -4.306 | -3.705 | -1.991 | -2.720 | -3.374 | -3.830 |
| | (2.843) | (3.158) | (3.162) | (3.176) | (2.979) | (3.179) | (2.991) | (3.266) | (2.838) | (3.177) | (3.337) | (3.309) |
| Projects in Development | 0.086** | 0.041 | 0.027 | 0.046 | 0.057 | 0.047 | 0.024 | 0.000 | 0.071 | -0.011 | -0.056 | -0.051 |
| | (0.043) | (0.055) | (0.046) | (0.055) | (0.044) | (0.057) | (0.046) | (0.057) | (0.046) | (0.058) | (0.054) | (0.064) |
| Total Assets (log) | 0.965** | 0.347 | 0.666 | 0.337 | 0.710 | 0.377 | 0.967** | 0.514 | 0.943** | 0.222 | 0.487 | 0.345 |
| | (0.452) | (0.442) | (0.457) | (0.442) | (0.458) | (0.450) | (0.452) | (0.455) | (0.456) | (0.453) | (0.468) | (0.474) |
| Financial Slack | 0.190 | 0.348 | 0.162 | 0.360 | 0.144 | 0.355 | 0.164 | 0.369 | 0.201 | 0.420* | 0.141 | 0.401 |
| | (0.219) | (0.245) | (0.223) | (0.246) | (0.223) | (0.245) | (0.222) | (0.253) | (0.220) | (0.254) | (0.228) | (0.258) |
| RoA | 2.872 | 0.505 | 3.534 | 0.650 | 3.053 | 0.632 | 2.612 | -0.475 | 2.814 | -0.201 | 3.273 | -1.314 |
| | (2.189) | (2.470) | (2.250) | (2.484) | (2.295) | (2.495) | (2.213) | (2.546) | (2.193) | (2.552) | (2.324) | (2.682) |
| Total Pipeline (PI-III) | 0.443 | 0.457 | 0.411 | 0.448 | 0.243 | 0.462 | 0.405 | 0.589 | 0.412 | 0.441 | 0.167 | 0.559 |
| | (0.404) | (0.399) | (0.408) | (0.398) | (0.417) | (0.400) | (0.409) | (0.415) | (0.405) | (0.407) | (0.422) | (0.424) |
| Chemistry Preference | -0.632 | -3.338* | -0.113 | -3.192* | -0.450 | -3.561* | -1.208 | -3.065* | -0.775 | -4.300** | -0.832 | -3.858* |
| | (1.433) | (1.816) | (1.500) | (1.928) | (1.486) | (1.828) | (1.415) | (1.853) | (1.454) | (1.881) | (1.526) | (2.040) |
| Failure | -0.920** | -1.025** | -0.838** | -1.061** | -1.076** | -1.027** | -0.972** | -1.007** | -0.930** | -1.321*** | -1.008** | -1.302** |
| | (0.407) | (0.464) | (0.426) | (0.469) | (0.429) | (0.464) | (0.420) | (0.472) | (0.409) | (0.501) | (0.449) | (0.516) |
| Non-research Partnership | 0.073 | 0.158 | 0.102 | 0.135 | 0.106 | 0.162 | 0.113 | 0.125 | 0.085 | 0.006 | 0.165 | -0.022 |
| | (0.094) | (0.167) | (0.098) | (0.169) | (0.101) | (0.168) | (0.099) | (0.168) | (0.096) | (0.183) | (0.107) | (0.191) |
| Cognition Biotech. | -0.082 | 0.037 | -0.078 | 0.039 | -0.079 | 0.039 | -0.084 | 0.062 | -0.085 | 0.029 | -0.083 | 0.049 |
| | (0.091) | (0.091) | (0.095) | (0.091) | (0.094) | (0.091) | (0.092) | (0.090) | (0.090) | (0.091) | (0.096) | (0.092) |
| Internal Research | | | 0.075*** | 0.006 | | | | | | | 0.063*** | 0.001 |
| | | | (0.022) | (0.011) | | | | | | | (0.023) | (0.012) |
| Research Contracts | | | | | 0.681*** | 0.099 | | | | | 0.515*** | 0.123 |
| | | | | | (0.171) | (0.283) | | | | | (0.176) | (0.301) |
| Research Alliances | | | | | | | 0.651*** | 0.705*** | | | 0.473*** | 0.641*** |
| | | | | | | | (0.170) | (0.209) | | | (0.177) | (0.217) |
| Technology Acquisitions | | | | | | | | | 0.238 | 0.957*** | 0.314 | 0.839*** |
| | | | | | | | | | (0.245) | (0.303) | (0.252) | (0.306) |
| Firm Fixed Effect | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| Year Fixed Effect | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| Log Likelihood | -199.41 | -171.83 | -192.26 | -171.47 | -190.28 | -171.56 | -190.87 | -165.40 | -198.96 | -166.06 | -180.08 | -161.30 |
| Observations | 591 | 561 | 591 | 561 | 591 | 561 | 591 | 561 | 591 | 561 | 591 | 561 |

* $p<0.1$; ** $p<0.05$; *** $p<0.01$

**Table 4: Robustness Checks: Conditional Fixed Effects Logit Estimates for Incumbents' Commercialization**

| DV: Commercialization | (13) MAbs IVs: 0/1 | (14) GT IVs: 0/1 | (15) MAbs IVs (2y) | (16) GT IVs (2y) | (17) MAbs IVs (4y) | (18) GT IVs (4y) | (19) MAbs 92- 02 | (20) GT 92-02 | (21) MAbs (ex HGP) | (22) GT (ex HGP) | (23) MAbs 98-08 | (24) GT 98-08 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R&D Intensity | -3.533 | -4.336 | -3.046 | -3.385 | -2.544 | -4.427 | -1.987 | -5.240 | -2.429 | -4.797 | -4.549 | -5.842 |
| | (3.031) | (3.291) | (3.369) | (3.241) | (3.394) | (3.505) | (6.848) | (4.800) | (3.454) | (4.258) | (3.983) | (4.892) |
| Projects in Development | 0.004 | -0.024 | -0.034 | -0.037 | -0.032 | -0.057 | 0.002 | -0.110 | -0.029 | -0.103 | -0.165** | -0.105 |
| | (0.047) | (0.062) | (0.052) | (0.062) | (0.055) | (0.065) | (0.099) | (0.090) | (0.067) | (0.097) | (0.072) | (0.090) |
| Total Assets (log) | 0.761* | 0.326 | 0.482 | 0.465 | 0.519 | 0.306 | 0.516 | -0.652 | 0.804 | -0.161 | 0.575 | 0.020 |
| | (0.458) | (0.466) | (0.464) | (0.469) | (0.465) | (0.477) | (0.768) | (0.870) | (0.559) | (0.559) | (0.810) | (0.654) |
| Financial Slack | 0.059 | 0.456* | 0.111 | 0.374 | 0.089 | 0.440* | 0.459 | 0.184 | 0.055 | 0.763** | 0.000 | -0.357 |
| | (0.227) | (0.255) | (0.227) | (0.257) | (0.227) | (0.263) | (0.356) | (0.354) | (0.265) | (0.349) | (0.391) | (0.356) |
| RoA | 2.648 | -1.131 | 2.594 | -0.181 | 3.751 | -1.341 | 2.934 | -6.321 | 3.808 | -2.275 | 5.581* | -1.338 |
| | (2.260) | (2.703) | (2.335) | (2.613) | (2.341) | (2.683) | (3.639) | (3.855) | (3.053) | (3.649) | (3.293) | (3.322) |
| Total Pipeline (PI-III) | 0.343 | 0.449 | 0.205 | 0.580 | 0.209 | 0.581 | 0.142 | -0.005 | 0.433 | 0.562 | 0.503 | 0.031 |
| | (0.426) | (0.418) | (0.422) | (0.425) | (0.420) | (0.424) | (0.513) | (0.606) | (0.532) | (0.545) | (0.785) | (0.560) |
| Chemistry Preference | 0.205 | -3.583* | -0.885 | -4.056** | -0.474 | -3.960* | -0.439 | -2.820 | -3.345 | -3.240 | 4.414 | -6.319** |
| | (1.585) | (1.918) | (1.506) | (1.990) | (1.558) | (2.058) | (2.196) | (3.039) | (2.181) | (2.996) | (3.274) | (2.705) |
| Failure | -0.950** | -1.275** | -0.948** | -1.094** | -1.105** | -1.360*** | -0.807 | -2.036** | -0.714 | -1.418** | -1.722*** | -1.427** |
| | (0.426) | (0.499) | (0.451) | (0.508) | (0.450) | (0.518) | (0.642) | (0.852) | (0.537) | (0.671) | (0.650) | (0.640) |
| Non-research Partnership | 0.139 | -0.002 | 0.131 | 0.070 | 0.154 | 0.013 | 0.106 | -0.380 | 0.082 | 0.100 | 0.162 | -0.127 |
| | (0.099) | (0.176) | (0.105) | (0.186) | (0.106) | (0.191) | (0.191) | (0.335) | (0.140) | (0.275) | (0.127) | (0.221) |
| Cognition Biotech. | -0.049 | 0.067 | -0.101 | 0.034 | -0.070 | 0.055 | 0.108 | -0.090 | -0.032 | 0.054 | -0.165 | 0.019 |
| | (0.091) | (0.092) | (0.100) | (0.092) | (0.096) | (0.092) | (0.162) | (0.169) | (0.104) | (0.107) | (0.122) | (0.110) |
| Internal Research | 1.054*** | -0.114 | 0.095*** | -0.003 | 0.046** | -0.003 | 0.102** | 0.010 | 0.054* | 0.006 | 0.065* | 0.005 |
| | (0.390) | (0.422) | (0.030) | (0.015) | (0.019) | (0.008) | (0.042) | (0.016) | (0.028) | (0.017) | (0.037) | (0.018) |
| Research Contracts | 0.982*** | 0.133 | 0.622*** | 0.126 | 0.521*** | 0.167 | 0.560** | 0.276 | 0.461** | 0.294 | 0.359* | 0.096 |
| | (0.290) | (0.372) | (0.193) | (0.328) | (0.161) | (0.281) | (0.285) | (0.378) | (0.201) | (0.402) | (0.215) | (0.410) |
| Research Alliances | 0.743** | 0.878*** | 0.432** | 0.656*** | 0.277* | 0.563*** | 0.508 | 0.490* | 0.616*** | 0.671** | 0.492** | 0.610* |
| | (0.312) | (0.324) | (0.181) | (0.237) | (0.159) | (0.195) | (0.309) | (0.272) | (0.217) | (0.281) | (0.207) | (0.341) |
| Technology Acquisitions | 0.109 | 1.205*** | 0.553* | 0.806** | 0.037 | 0.722** | 0.330 | 0.864* | 0.477 | 1.315*** | 0.382 | 0.867** |
| | (0.389) | (0.383) | (0.304) | (0.332) | (0.233) | (0.295) | (0.436) | (0.525) | (0.313) | (0.475) | (0.310) | (0.365) |
| Firm Fixed Effect | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| Year Fixed Effect | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| Log Likelihood | -184.45 | -160.56 | -181.13 | -163.22 | -182.82 | -162.86 | -102.22 | -95.49 | -122.02 | -91.47 | -88.30 | -91.22 |
| Observations | 591 | 561 | 591 | 561 | 591 | 561 | 338 | 276 | 395 | 327 | 307 | 300 |

* $p<0.1$; ** $p<0.05$; *** $p<0.01$