Clinical Trials, Innovation and Approaches to Ambidexterity in Pharmaceutical Startup Companies

MSc in Innovation and Entrepreneurship

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Abstract

The author investigates how the clinical trial process affects innovation in pharmaceutical start-up firms. A deductive qualitative case study methodology is utilized to investigate three pharmaceutical start-up firms that are conducting late stage (phase II or III) trials.

Key assumptions are that pharmaceutical start-ups must simultaneously pursue exploration and exploitation in different domains while operating under the resource constraints typical for start-up firms. Research identifies two key domains of ambidexterity, technology vs market, that are known from existing literature to have conflicting demands.

Pharmaceutical firms were selected because the pharmaceutical industries lack strong competitive market forces. Lack of strong competitive market forces are assumed to reduce the exogenous sources of interference, making analysis of internal factors easier.

Key findings are that early initiation of exploration in the market domain is critical for success in new product development among pharmaceutical firms. The more innovative a product is, the more difficult and important early market exploration becomes. Pursuit of balanced exploration and exploitation is also found to positively moderate economic success in the investigated cases.

Previous research indicates that exploration in one domain will be balanced by exploitation in other domains. Domain specific ambidexterity in pharmaceutical start-ups is shown to differ from existing literature, as both exploration and exploitation activities occurs simultaneously in multiple domains.

Keywords: Innovation, pharmaceutical industries, life science, management, ambidexterity, domain specific, exploration, exploitation, learning.
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1 Introduction

Pharmaceutical start-up firms operate in a strictly regulated environment where the clinical trial process leading up to marketing approval of a treatment constrains start-up innovation. This thesis investigates how pharmaceutical start-up firms can balance market vs technology domains and maintain a simultaneous balance between the learning processes that contribute to exploration vs exploitation.

Particularly for start-up firms, the clinical trial process is seen as a synthesis of all the challenges of bringing a new technology to the market, making it appropriate for investigation of innovation in clinical trial processes. Little work has been done looking at the clinical trials process as an area of innovation.

On a general note, literature has shown that all start-ups have a limited probability of survival compared to established firms (Freeman, Carroll, and Hannan 1983). The ‘liability of newness’ term was first coined by Stinchcombe (Stinchcombe 1965). Stinchcombe argues that new organizations suffer from a variety of issues such as resource poverty, insufficient partner networks and lack of legitimacy. It is generally accepted in literature that these challenges are made even more difficult for technology firms (Nesheim 2000). In contrast to established firms, typical start-up firm growth is also especially limited by a lack of resources (Penrose 1995). All of these combine to create strategic hurdles that necessitates a focus on firm survival rather than profitability (Graebner 2004).

The cost of new product development for pharmaceutical products has been estimated to an average of 828 million USD for each successful treatment candidate (DiMasi, Hansen, Grabowski, et al. 2003). While expensive, the bigger challenge is an industry-wide low success rate of 9% (Hay et al. 2011) or less in clinical trials for new product candidates. Other industry-specific issues are management of complex clinical trials processes (Hara 2003), thirteen-year-long product development cycles (DiMasi, Feldman, et al. 2010) and a regulatory environment that acts both as a market entry barrier and as a limit on market size.

Problem Statement

All of the above challenges creates a start-up firm environment where the clinical trial contains almost all the elements of success or failure, including innovative thinking in core technologies, the execution of clinical trials and the market approach.

While it will be difficult for individual firms to overcome industry wide issues such as high failure rates and difficulties of finding funding, a firm can still influence its own fate through other mechanisms such as culture, leadership, partnerships or other similar “soft” factors. Given the industrywide issues, start-up firms in particular have an increased need to balance short term and long term considerations during the early start-up stages to increase their survival odds and to safeguard their future economic potential.

The research started with a wide research question “What determines the success
or failure in clinical trials for start-up pharmaceutical companies?”. Based on data gathered through a pilot interview, relevant theoretical approaches in existing literature were chosen and propositions generated from theory were tested on the gathered primary source data.

Relevant theories in literature are ambidexterity theories that address how to reconcile the paradoxical natures of the learning processes needed to deal with long term vs short term considerations. Literature have shown that ambidextrous firms outperform other firms (Gupta, K. G. Smith, and Shalley 2006; He and Wong 2004; Lubatkin et al. 2006) and that ambidexterity challenges are relevant to the investigated cases.

This thesis addresses which feasible approaches for a pharmaceutical start-up will enhance their odds of success by looking at the firms in the context of a clinical trial process. The author extends the concept of domain specific ambidexterity by Rosenkopf and Lavie (Lavie and Rosenkopf 2006) to include two domains, the Technology and Market domains. Domain specific approaches to ambidexterity is shown to explain why the transition from an initial technology focus to market focus remains a challenge for pharmaceutical start-ups.

Structure of the Thesis

The thesis is structured based on Wilson’s recommendations (Wilson 2010). First, the empirical context (see section 2, page 4) is introduced, followed by theoretical framework (see section 3, page 8). Within the theoretical framework, the propositions are presented (see pages 14, 17 and 17). Theoretical framework is followed by methodology (see section 4, page 17) and case study findings (see section 5, page 23). Finally the thesis discussion (see section 6, page 36) and overall conclusions (see section 7, page 41) are presented.

2 Empirical Context

In pharmaceutical industries the new product development process is subject to a strict regulatory environment where governmental agencies grant or deny an permission to sell and market a treatment. For a treatment to gain an market approval, the prospecting medical treatment must first pass a carefully staged testing and documentation process (clinical trial process) consisting of three main stages (phases).

2.1 The Clinical Trial Process

After the Thalidomide tragedy in 1961, the drug development and testing regimes became strictly regulated by governmental agencies such as the US Food and Drug Administration (FDA) and European Medicines Agency (EMA). Prior to the tragedy, regulatory approval was given by default if no response from the US Federal Food and Drug Administration (FDA) was given within 30 days. After the tragedy, FDA approval has to be given
explicitly (Kelsey 1988).

The FDA’s (and similar agencies’) main purpose is to protect public health, and these regulatory agencies are involved with all three phases of clinical trials culminating in a granting of a marketing approval (or rejection). Among the governmental agencies, the FDA is considered the critical regulatory agency as approval grants access to the US market and an FDA approval simplifies approval from other non-US agencies.

Initiating a clinical trial is done by the company but in practice all start-ups outsource the trial execution to contract research organizations (CRO). Each phase of a clinical trial is designed with feedback from and evaluated by a regulatory agency. Final evaluation depends on a treatment’s safety profile, its clinical benefit and societal benefit as documented during the three phases.

Testing of medical and pharmaceutical treatments is divided into two categories called ‘pre-clinical’ and ‘clinical’ trials. All trials not conducted on humans are considered pre-clinical trials. The clinical trials are divided into several phases, ‘Phase I’, Phase II’, ‘Phase III’. In addition there can be clinical trials occurring after final approval, often called ‘Phase IV’ trials. Of relevance for this thesis are the Phase I-III trials as these are considered the biggest challenges for pharmaceutical start-up firms.

The success of each clinical trial phase is determined by how well each phase achieves its predetermined ‘End Points’ (EP), i.e. the clinical success criteria. These EP are established by the beginning of a clinical trial and modifications are seldom possible after initiation of a clinical trial phase. Secondly, a product that achieves its EP goals can only gain permission to be marketed and sold on indications (diseases, conditions, patient groups) that the trial EP were designed to test. So, while safety and benefits are a necessary requirement for FDA approval, the choice of appropriate EPs have a profound impact on the economic success as it defines the legally permissible target market (often called having a ‘label’ for that treatment application).

2.2 Off-label Sales and Orphan Drug Status

While having a ‘label’ is critical, this does not preclude the possibility of market strategies that utilizes off-label sales to generate profits. This is due to doctors being allowed to prescribe drugs or treatments to patient groups not covered by the label. This is commonly referred to as ‘off-label’ sales in industry jargon, but companies are not permitted by the FDA (or other agencies) to market such usage. One such example is the compound Sildenafil that was originally developed to treat a rare heart problem. Sales of Sildenafil skyrocketed when doctors started to prescribe it for erectile dysfunction. FDA required Sildenafil to conduct new clinical trials to test for this application, but it took years before the compound gained a label for erectile dysfunction under the trade-name Viagra (Sherr et al. 2000).

The US Orphan Drugs Act (ODA) was passed in 1983, to reward firms for engaging in R&D of treatments for rare ailments where no treatments are currently available. An
ODA status provides a firm with additional legal anti-competitive protections by granting market exclusivity for a number of years. While the ODA does spur R&D on rare diseases, according to Yin et al. (W. Yin et al. 2009) it also permits treatment development to target initial small sub-populations within larger populations with the same medical condition, as long as these sub-populations are narrowly defined to fall within the legal requirements for an ODA status.

Off-label sales and ODA status are possible sources of revenue that start-ups can take into consideration during the clinical trials process. However, to generate off-label sales from an ODA requires at least a single approved product on the market, something that few start-ups have. As such, the possibility of off-label sales and an ODA label can lower the barriers of market entry but also serves to increase the complexities of how to conduct a start-up’s first new product development process. For a start-up this added complexity requires more long term planning (and managerial resources) without providing short term revenues to offset the added resource burden.

2.3 Regulatory Market Barriers

Start-ups in these industries have limited resources to conduct clinical trials and have to focus on developing a single product from their core technology. A pharmaceutical start-up’s viability (both short and long term) as a for-profit entity is then contingent on overcoming the market entry barrier that the clinical trial process represents. Usually a start-up will out-license a finished (or almost finished) product to larger pharmaceutical companies where revenues (royalties etc.) are contingent on a the treatment gaining a final regulatory market approval.

While gaining an approval represents an market entry barrier, approval also defines the market size and potential revenues. This is due to several regulatory requirements for a final approval. Among the important requirements are a) a well defined patient population, b) the new treatment must either show substantial improved medical benefits or c) be equal to but more cost efficient compared to existing treatments.

Overcoming the market entry barriers and defining a profitable market size is then not only a question of technology or just a clinical trial execution issue, because market size, pricing and market demand is shaped by how the new product candidate’s market is defined during the clinical trial process. That is to say, success in a clinical trials process also requires a balanced focus between market and technology domain considerations.

2.4 Consequences of Trial Failure

Typically, the total cost of conducting clinical trials for one treatment are in the range of 180.2–322.4 million USD (with a 95% confidence interval) (DiMasi, Hansen, Grabowski, et al. 2003). While a 2011 review by Morgan et al. (Morgan et al. 2011) questioned the transparency of 10 out of 13 published cost estimates, including DiMasi et al 2003 paper,
this does not invalidate the use of DiMasi et al, as the more reliable transparent cost estimates are still large (in the range of 113-206 million USD) and the estimated failure rates by DiMasi et al (DiMasi, Feldman, et al. 2010) remain largely unchallenged. Industry analysts Hay et al (Hay et al. 2011) reported at the US Biotechnology Industry Organization conference 2011 that the clinical trial approval rate is 11% from phase I to III, and even after having passed through all three main phases, gaining a final approval is only 80% probable (a total approval rate of 9%). The average failure rate given by DiMasi et al (DiMasi, Feldman, et al. 2010) supports this estimate, though the majority of the treatment classes described by DiMasi et al have even lower success rates, in the range of 3%-5%. The discrepancy is due to a small number of treatment categories increasing the average with success rates in the range of 15%.

Failure in the later stages is found to be particularly disastrous for two reasons from a single start-up’s point-of-view. The later in the clinical trial process a phase fails, the larger the loss of investment and the less time remaining to redo a trial before the firm loses patent protection on their new product candidate. Urbig et al (Urbig et al. 2013) show that bio-tech firms face a larger loss of shareholder trust after a failure in late clinical trial stages than a failure in the early stages. Failure in early stages is on the other hand somewhat expected, especially in phase I. According to DiMasi et al (DiMasi, Feldman, et al. 2010), such failures are in some cases a deliberate part of the new clinical trial process before continuing to the more expensive and difficult phase II and III.

2.5 Clinical Trial Model

For start-ups the typical development cycle (see figure 1) for the first product is initiated by a scientific discovery; typically the discovery is made before the start-up is founded. Pre-clinical research is then conducted to develop a new product candidate before the clinical trial process is initiated. Approval is occasionally given contingent on a firm performing additional post-approval clinical trials (phase IV trials). The average time-frame for successful new product development is thirteen years from entering the pipeline (pre-clinical) until gaining marketing approval (post-phase III) (DiMasi, Feldman, et al. 2010).

As previously mentioned, the core of a clinical trial process is the phases I, II and III, usually described as a linear progression from I to III (see figure 1). However, in reality the process is non-linear with multiple levels of feedback, according to Takuji Hara (Hara 2003) in his book 'Innovation in the Pharmaceutical Industry'.

![Figure 1: The clinical trial process](image)

Takuji Hara identified four areas of interest as part of the clinical trials process; ’The
shaping of the compound’, ‘the shaping of the application’, ‘the shaping of the organizational authorization’ and ‘the shaping of the market’. Between each area there are multiple feedback cycles, supporting Hara’s argument that the linear model of technological change is flawed in the context of pharmaceutical new product development.

With Hara in mind, each phase as seen in figure 1 will be viewed as rough milestones rather than definite goal achievements. For example, failure in one milestone of the trial cycle could set a firm back to any preceding milestones but also contribute critical information despite being a ‘failure’. While the simplified model is often adequate, the activities that support progression through a clinical trial process do not need to be confined to one specific phase.

3 Theoretical Framework

3.1 Balancing Exploitation vs Exploration

As a consequence of resource limitations, high R&D costs and low probability of success, the question of how to balance exploration vs exploitation activities becomes a critical issue for pharmaceutical start-ups.

March (J. G. March 1991) introduces the notion that ambidexterity is not a question of trade-off, but rather depends on the ability to simultaneously maintain paradoxical thoughts. Ambidexterity theories then addresses the issues of simultaneous balancing between disparate activities. Some examples are such things as manufacturing efficiency and flexibility (Adler, Goldoftas, and Levine 1999; Carlsson 1989), low-cost vs differentiation strategies (Porter 1980; Porter 1996) or pursuing both incremental and radical innovation (M. Tushman and OReilly 1996).

In the context of ambidextrous learning activities, exploitation activities are those that refine existing knowledge or strengthen existing capabilities (J. G. March 1991). For pharmaceutical start-ups, exploitation activities are related to how to keep a specific new product candidate moving through the clinical trial process, e.g. refining technology, documenting the clinical process, maximizing the return from existing partnerships, building the distribution and production capability to sell and market a product or maintaining the relationship with an out-licensing partner.

Exploration activities are activities that involve acquiring knowledge outside existing knowledge domains or acquiring new capabilities (J. G. March 1991). For pharmaceutical start-ups exploration is related to determining what options are available from the technology or the market, e.g. discovering new scientific mechanisms, identifying the conditions that a new scientific technology could treat, identifying unmet market needs, identifying potential out-licensing partners and learning how to approach possible strategic partners.
3.2 Antecedents of Ambidextrous Learning Behavior

As development of pharmaceutical treatments are knowledge intensive activities, the essence of a clinical trials process is all about learning; learning about the compound, learning about the market, learning how to apply the compound, learning how to communicate its value, and so forth.

Learning processes are found to not be without challenges, as research has shown that prior learning activities lead to a 'Myopia of Learning' (D. Levinthal and J. March 1993). A prior learning process leads to accumulation of knowledge, but future experience is then filtered and discarded when it does not fit with the existing knowledge. Nor does learning automatically lead to novel knowledge (Levitt and J. March 1988) as it takes effort to break out of existing patterns. Levitt and March (Levitt and J. March 1988) suggest that learning processes are slow and lead to abrupt changes rather than incremental changes (i.e. they are punctuated equilibriums). Nor is it trivial to switch between different types of learning behaviors, as a study of vicarious group learning in pharmaceutical in-licensing teams concludes that new groups learn by imperfect imitation and adaptation of routines from other groups (Bresman 2013) rather than 'copy exactly' routines.

The type of learning behavior also influences the balance of exploration vs exploitation, rather than it being an absence of learning (Baum, Li, and Usher 2000). Given that learning myopia increases the cost of switching between learning behaviors, it leads to a tendency towards extremes with regards to exploration vs exploitation (Ghemawat and Costa 1993). Ghemawat and Costa find that firms with exploration (exploitation) focus tend to become better at the same, and the better they become at exploration (or exploitation) the more difficult it is for them to relearn/learn the corresponding opposing activity.

The characteristics of the different learning types associated with exploration vs exploitation are as follows: Learning that supports exploitation is characterized by 'local search' activities (same geographic, same demographic, existing domain knowledge, strengthen existing partnerships). Learning that supports exploration is characterized by 'long jump' activities (new geographies, different demographic, new domain knowledge, build new partnerships) (D. A. Levinthal 1997).

As part of learning feedback mechanisms, exploitation is further encouraged by 'single loop' learning where actions are modified by the difference between expected and obtained outcomes. In contrast, exploration is further encouraged by 'Double loop' learning where the initial assumptions and policies are reviewed (questioned) when differences occur between expected and obtained outcomes (Argyris and Herbane 2005). Existing literature concludes that learning is an important factor when overcoming any ambidexterity challenge.
3.3 Technology and Market Domain Ambidexterity

While the learning differs between exploration and exploitation activities, initially such learning was assumed in literature to not significantly differ between learning in different domains; effectively, that the same cognitive processes occurred when conducting exploration in for example the technology or the market domain.

While similar activities (exploration or exploitation) in different domains have many similarities, there are also indications that a focus on the technology domain does not alleviate a lack of market oriented focus (D. Ford and Ryan 1981). Nor does a market oriented focus drive technological innovation; in fact a market oriented focus is found to impede technological innovation, especially radical (Zhou, Yim, and Tse 2005) or disruptive innovations (Christensen and Bower 1996). While exploration (or exploitation) within one domain have similarities with exploration (exploitation) in another domain, the domain specific differences are non-trivial and have to be taken into account when discussing new product development, especially so for start-up firms as they have little initial experience on addressing the particular technological or market challenges created by their core technology.

The notion of domain specific ambidexterity is introduced by Lavie and Rosenkopf (Lavie and Rosenkopf 2006). Lavie and Rosenkopf identify conflicting conclusions in existing literature on the connection between firm size and exploration/exploitation:

“Prior research on the antecedents of exploration and exploitation have produced inconsistent evidence because each study examined exploration and exploitation within a single domain, disregarding the conflicting organizational pressures that influence learning in various domains.” -(Lavie and Rosenkopf 2006)

For example, one empirical study finds that exploitation (at the cost of exploration) increases with firm size (Rothaermel and Deeds 2004) while another empirical study finds that exploration increases with firm size (Beckman, Haunschild, and Phillips 2004).

While Lavie and Rosenkopf uses an empirical study of alliance formation in the software industries to provide empirical evidence for their theory, their concept of domain specific ambidexterity is also applicable to internal (intra) firm factors. Based on this, domain specific ambidexterity is extended to the pharmaceutical industries and used to test for intra-firm factors.

3.4 Market Exploration Timing for Pharmaceutical Start-Ups

Since pharmaceutical start-ups are often initiated as a result of a scientific discovery, it is assumed that a majority of firms have a primary focus on technology R& D, while more market oriented activities enter the picture somewhat later. While this is not necessarily always true, it is a reasonable assumption for a pharmaceutical start-up.
DiMasi et al (DiMasi, Feldman, et al. 2010) report that the odds of successfully completing clinical trials increase when firms conduct multiple phase I trials. The possible explanation for multiple phase I trials are that these trials are designed with the primary goal of providing data rather than achieving the trial EPs needed to continue to phase II.

Figure 2: Activities in a clinical trial process

Tying together the two assumptions for pharmaceutical start-ups allows development of an preliminary model as depicted in figure 2. Bear in mind that this is a preliminary model where the exact placement of activities remain subject to change depending on the data gathered.

Drawing on learning behavior and the existence of learning barriers between activities, it is reasonable to assume that the barriers to learning are lower when learning similar activities between different domains (Technology vs. Market) or when learning disparate activities within the same domains (see figure 3).
The theoretical framework of interest consists of several phases and domains, as illustrated in Figure 3. The phases include pre-clinical (Phase I), clinical (Phase II), and post-authorization (Phase III). The domains are divided into technology and market exploitation. Within the same domain, there are exploration and exploitation activities.

Figure 3: Barriers to transfer of firm focus is lowest within domains or between similar activities

The rationale for the two assumptions are: while exploration (or exploitation) between domains share similarities, the knowledge base they build upon differs. It is however intuitive that if people have personality traits (curiosity, ‘outside-the-box thinking’) that make them suited for exploration, such traits reduce the difficulties of acquiring knowledge in previously unfamiliar domains. The same argument also applies to learning that supports exploitation activities in new unfamiliar domains. It is then reasonable to assume the difficulties of learning exploration (or exploitation) within a new domain will be reduced if a firm has retained within an existing domain its capabilities to do both exploration and exploitation.

When operating within the same domain the end result of lower learning barriers remains the same, but for different reasons. While switching between domains does not build upon existing knowledge, remaining within a domain does. For example, if a person’s prior focus has been on exploration, learning new behaviors that supports same domain exploitation builds upon an existing knowledge base.

As a consequence of this, the lowest barriers to learning new behaviors exists between similar behaviors (exploration <-> exploration, exploitation <-> exploitation) or within a domain (technology <-> technology, market <-> market). Supporting the assumption of lowered learning barrier both within and between domains are the prior findings that high tech start-up firms who have a higher degree of market orientation (Kyriakopoulos and Moorman 2004) and firms with ambidextrous founding teams (Beckman 2006) outperform those who do not.

However, given that a product made by a pharmaceutical start-up is novel in a technological sense, there can be no perfect a-priori understanding about either the technological or the market domain. Since start-up firms are resource constrained, there has to be
a limited number of possible pathways that a typical pharmaceutical start-up can utilize to reach the market. As such pharmaceutical start-ups are constrained to a trajectory as depicted in figure 4 for several reasons.

Firstly, the initial focus on technology ensures that most start-up firms emerge in the 'Technology Exploration' quadrant. Then, resource demands of technology exploitation will force most start-up firms to focus on the technological aspects of new product development (step A, figure 4) during the initial stages. As a new product candidate matures during the clinical trials stages, information gathering during technological exploration and exploitation combines with stakeholder demand (shareholders, customers, regulatory agencies, etc.) to trigger an increase in market orientation and subsequent market exploitation (step B, figure 4). After having identified possible market applications and leads, this will then again trigger a increased focus on market exploitation to complete the new product development process (step C, figure 4).

An industry perspective published in Nature biotechnology in 2011, Booth and Salehizadeh (Booth and Salehizadeh 2011) argue that pharmaceutical start-up companies require a more hands-on investor approach and more concentrated bets compared with other industries. Of great salience is Booth and Salehizadeh’s conclusion that;

“Although scientific and/or engineering failures can certainly plague some technology deals, a far more common cause is market failure: the inability to create and sustain a competitive advantage in a marketplace with a particular technology-related product or service.”

Addressing market failure is then the critical factor when looking at how new product development in a clinical trial process could succeed. Given the models discussed so far, the increased market orientation will occur when a firm moves from technology exploitation to market exploration (see step B in figure 4).
The step from technological exploitation to market exploration will then be the logical failure point when addressing market failure. As previously argued, the lowest barriers to learning will be aligned within domains or between similar activities (exploration <-> exploration, etc). When going through 'step B' (figure 5), a start-up firm will then have to overcome a 'double learning curve' in the sense that they have to learn within a new domain (Technology -> Market) while simultaneously (re)learning exploration behavior after a period of focus on exploitation.

Failure to address the 'double learning curve' can occur in multiple ways. Firstly, failing to acquire knowledge within the new market domain will cause a firm to underestimate the market in relation to new product development. On the other hand, failing to put sufficient emphasis on market exploration ensures that viable market (profit) opportunities are not identified. In both cases, a 'myopia of learning' will occur that hurt the survival chances of a start-up firm.

Within the framework of ambidexterity theory, the solutions to the 'double learning curve' is to use approaches that balance the learning behaviors so as to support both exploration with exploitation. If done correctly, this will lower the difficulty of simultaneous crossing within and between domains.

To complete a clinical trial process successfully requires at least that a firm identifies one single viable market application/approach. While a single viable application is sufficient, the more potential market application leads they can pursue before entering market exploitation, the better their chances of identifying more profitable market applications. Since there can be a significant time duration between initiation and completion of a clinical trial process, the somewhat easy solution is to pick any approach that reduces the time differences between technology exploration and market exploration. This leads to Proposition 1: The earlier a pharmaceutical start-up firm engages in market exploration, the more likely a clinical trial process leads to commercial success.
While proposition 1 is simplistic and does not directly address ambidexterity challenges, it is utilized as a starting point for further investigation on what approaches to ambidexterity are viable for pharmaceutical start-up firms.

### 3.5 Feasible Approaches to Ambidexterity for Pharmaceutical Start-Ups

The simplest ambidexterity approach is to have none, namely the ‘single focus’ approach (Porter 1996; J. D. Ford and L. W. Ford 1994; Lewis 2000). In the case of pharmaceutical start-ups, two reasons argue in favor of a single focus on exploration. Firstly, pharmaceutical start-ups outsource the majority of technology oriented exploitation tasks in clinical trials to Contract Research Organization (CRO). 90% of pharmaceutical firms (Hughes 2004) did some sort of outsourcing as part of their new product development. Secondly, pharmaceutical start-ups more often than not utilize an out-licensing strategy for their late stage products, so a licensing partner can take on the market oriented exploitation activities. However, in reality firms can not avoid spending time and effort on technology exploitation activities, because outsourcing runs afoul of the principal-agent when outsourcing to CROs (Lovatto and Sibony 2006). Bryde (Bryde 2007) stresses that outsourcing any part of a clinical trial process requires constant effort to set up and manage. Given that outsourcing of clinical trials requires management effort, a “pure” single focus approach is not possible for pharmaceutical start-ups. (Unless of course a new product candidate is outsourced before any clinical trials are conducted.) Discounting a single focus approach for the vast majority of pharmaceutical start-ups, what are the remaining approaches?

Temporal approaches (McDonough and Leifer 1983; Adler, Goldoftas, and Levine 1999; Duncan 1976) to ambidexterity involves putting current exploitation (or exploration) activities on hold when pursuing the opposite exploration (exploitation) activity. For example, in the context of pharmaceutical start-ups, if exploration becomes necessary, any existing exploitation would be put on hold while pursuing the exploration opportunity. However, a temporal approach is unfeasible for the same reason as a ‘single focus’ approach, because management of an ongoing clinical trial process cannot be abandoned.

The remaining approaches all attempt to ensure that exploration and exploitation occur simultaneously within an firm. Structural approaches (J. R. Galbraith 2002; Drucker 1999; M. Tushman and OReilly 1996) to ambidexterity argue the need for a structural separation of exploration vs exploitation into different business units. While structural ambidexterity is clearly feasible in established firms, (Gibson and Birkinshaw 2004) points out that this leads to an coordination cost (in managerial and financial terms) between the business units, a burden that start-up firms seldom can afford.

The remaining two, task partitioning and contextual approaches, share many characteristics and exist along the same continuum rather than directly oppose each other. The task partitioning approach (Hedlund and Ridderstrale 1997; Adler, Goldoftas, and Levine
on ambidexterity means that one group takes on a more ‘organic’ role while another group has a more ‘mechanistic’ role. By ‘organic’, Hedlund and Adler meant situations where information is ambiguous in nature and evaluation of such information relies on tacit (intuitive) knowledge. By ‘mechanistic’ they meant situations where information evaluation relies on explicit (rule based reason) knowledge. Task partitioning approaches are characterized by multiple organizational structures within the same group, for example a mix of hierarchical structures with flat structures where the different structures address each of the different roles.

Contextual ambidexterity approaches (Gibson and Birkinshaw 2004) emphasize that successful balance between exploration and exploitation could be driven by voluntary individual behavior rather than organizational structures. In contrast to task partitioning, every employee is encouraged and expected to contribute to exploration and exploitation regardless of what their main assignments are. As such, the role of organizational structure, culture and leadership/management is not to formalize a structure, but rather to reduce barriers for sharing of knowledge, enhance idea generation, encourage discussions and make employees draw on their own personal external networks.

One notable indicator of contextual approaches to ambidexterity are the two traits, ‘alignment’ and ‘adaptability’ across an entire business unit (Gibson and Birkinshaw 2004). Alignment means that people work towards the same goal, while adaptability is the capacity to reconfigure activities to quickly address changes in the task environment. Contextual ambidexterity occurs when individuals are encouraged to make their own judgments about how to divide their time between the conflicting demands of alignment and adaptability. (Duncan 1976; McDonough and Leifer 1983; M. Tushman and OReilly 1996)

To overcome the “double learning curve” challenge when going from technology exploitation to market exploration, the emphasis have to be on approaches that support exploration learning when entering new domains. Building in propositions 1, the logical extension of minimizing separation between technology- and market- exploration would be to use approaches that simultaneously balance exploration with exploitation activities within the firm. Given the previous discussion on approaches to ambidexterity, pharmaceutical start-ups will then be constrained to utilize task partitioning or contextual approaches to overcome the ambidexterity challenge.
This leads to **Proposition 2**: Utilizing a task partitioning or contextual approach positively moderates the likelihood of a clinical trial process leading to a commercial success for pharmaceutical start-ups.

Task partitioning delegates responsibility and execution of exploration activities to a minority while the majority of the employees largely remains single focused. As such, utilizing an task partitioning approach will not not fully encourage full utilization of the resources available to a firm as it permits people to engage in a limited ’not invented here’ thinking (or more precisely, ’somebody else is taking care of it’ thinking).

In the case of pharmaceutical start-ups going through ’step B’, the challenge would be in learning exploration. To maximize both search and sense-making in a small firm, all levels of firm employees have to be engaged to encourage learning behavior and knowledge flow that will enhance exploration within the new domain.

Contextual approaches to ambidexterity maximize exploration capability when currently pursuing exploitation, as every employee is encouraged and expected to engage in both types of learning behavior. As such, firms using contextual approaches should outperform firms utilizing task partitioning approaches.

This leads to **Proposition 3**: Utilization of a contextual approach has a greater positive moderating effect than a task partitioning approach on the likelihood of a clinical trial process leading to a commercial success.

### 4 Case Study Methodology

In the case of this thesis, a case study methodology is chosen to investigate multiple firms currently engaged in clinical trials. Case study methodology is a qualitative method best applied to answering “how?” and “why?” questions when looking at contemporary events. It is important to keep in mind that the findings of a qualitative study cannot be generalized, nor is this the goal of such research. The goal of case study research is not to prove or disprove generalized assumptions about a population, but rather to generate a more in-depth understanding of causation within the sample units or to generate new
insights that are otherwise hard to generate from empirical data. (R. K. Yin 2008; R. K. Yin 1981)

While quantitative research methodology has well established best practices grounded in standardized statistical approaches, the same could not be said to exist for case study methodologies. There are however some recommended best practices as described by Yin (R. K. Yin 2008) and Eisenhardt (Eisenhardt 1989).

4.1 Case Study Approach

Eisenhardt (Eisenhardt 1989) recommended researchers to include elements of grounded theory (Glaser and Strauss 1967) in deductive case study methodologies, meaning interviews are largely done prior to the development of propositions. However, having no pre-conceived theory does not preclude the necessity of doing preparatory work. Both Yin and Eisenhardt recommend that research question and interview protocols should be prepared based on preexisting constructs found in existing literature. Furthermore, not having a “theory to prove” also necessitates narrowing down the case sample to an manageable size by using non-theoretical constructs. As Eisenhardt (Eisenhardt 1989) recommends, prior to conducting interviews a research question is defined, with pre-defined dependent variables, (innovation in... success/failure of..) and furthermore, the case sampling criteria is also narrowly defined.

The desired case sample is defined to only include firms who fulfilled all of the criteria; a) being heavily focused on R&D, b) having few (or none) prior products on the market and c) currently conducting phase II or III clinical trials (see figure 7). In other words, a sample population consisting of pharmaceutical start-up firms conducting phase II or phase III clinical trials.
Conducting clinical trials

Few prior products

R&D focused

SME pharma startup

In phase II/III

Figure 7: Defined population sample from Research Question

The rationale behind the three sample criteria are as follows; criteria a) and b) select for case firms who are both resource constrained and have most of their “eggs in one basket” (i.e. pharmaceutical start-ups). Criteria c) ensures that each firm will have had the time to build up experience with conducting clinical trials and would still retain such knowledge in-house. While not part of the sampling criteria, the sample size is further constrained by logistical/practical considerations to only include Norwegian firms.

To ensure that theory building and propositions will not be biased towards a single case, a multi-case study is conducted. Multi-case studies are considered to be more reliable sources of insight as they permit a higher level of cross-pattern matching (R. K. Yin 2008; R. K. Yin 1981).

According to Yin (R. K. Yin 2008; R. K. Yin 1981), in multi-case studies each case should be treated as separate experiments rather than individual samples. Yin cautions that the usage of multiple case units in a multi-case study should not be confused with the multi-unit sampling logic behind quantitative methodologies. Each case is to be treated as separate experiments because all possible variables in each case cannot be compared between cases, nor is the sample size large enough for the utilization of a random sample approach.

Since sampling logic cannot not be applied to case studies, the goal of gaining an deeper understand of causation can also be simplified with the right choice of cases.
Eisenhardt (Eisenhardt 1989) recommends that cases should be further selected for an emphasis on their differences and stark contrasts to aid in theory building. With contrasting cases, the resulting propositions will be made easier to explain and exemplify. Equally important, clearly articulated propositions grounded in real world examples will be easier to test as hypotheses in future quantitative research.

4.2 Data Collection

Eisenhardt and Yin recommends utilizing multiple sampling methods such as interviews, archival information, direct observation or internal documentation. Direct observation was ruled out as too time consuming.

Accessing archival information and internal documentation from the cases was also deemed to be unfeasible. Firstly, gaining access would require very high levels of trust from the individual firms, internal documentation being an important part of the regulatory filings during clinical trials, making them highly sensitive with regards to competitors, shareholders and stakeholder interests. Even if such information was made available in the form of archival information, analyzing such data would be prohibitive due to the sheer volume and complexity of the data utilized in clinical trials. As described by Pettigrew (Pettigrew 1990) (when discussing case studies), there is an ever-present danger of “death by data asphyxiation.”

A semi-structured interview method was chosen due to its balance between allowing natural conversation flow and the need for a structured approach. As part of the semi-structured interviews an interview protocol was developed a-priori. A draft interview protocol was then tested with a pilot interview on a serial entrepreneur within the pharmaceutical industry. Based on feedback from the entrepreneur the interview protocol was revised before conducting further interviews. The interview protocol was then used without alterations throughout all the interviews to ensure consistency (see Appendix). Yin (R. K. Yin 2008; R. K. Yin 1981) cautions that an interview protocol is only intended for the researcher and should be used as an rough guideline for conducting interviews. The interview questions is presented as far as possible as open-ended questions as part of a natural free-flowing conversation.

Given the sampling criteria and practical considerations the geographical location for sampling was limited to Norway. Possible candidate firms were identified through biotechnology trade associations memberships leading to seven possible candidate firms that fulfill the sampling criteria. A letter of introduction (see Appendix) was prepared before contacting each firm, as recommended by Yin (R. K. Yin 2008; R. K. Yin 1981).

Success/failure of clinical trials is an industry wide phenomena that is dealt with on the level of each individual firm. To ensure that the unit-of-analysis is kept on a firm level, multiple individuals within each firms were interviewed to reduce source bias.

All seven candidate firms were initially contacted by phone. During initial contact, one firm was discovered to have been liquidated and remaining IP having been sold.
A second firm responded that they did not currently conduct any clinical trials, nor did they retain any staff with such experience. Among the remaining five candidates, three firms responded positively, all respondents being headquartered in the Norwegian capital region.

Given the existence of an nascent oncology industry cluster in the capital region, two out of three respondents are in the field of oncology treatment. The third candidate is in the field of cardiovascular treatment. From this point, the cases will be referred to as Alpha, Beta and Gamma.

One pilot interview and seven primary source semi-structured interviews were conducted. Only the seven primary sources were used as basis for case findings, discussion and conclusions. Primary sources are all mid-level managers working daily within clinical trial management and/or business development. All of the sources received a copy of the signed letter of introduction and were promised anonymity before interviews were conducted. Names (or individual identification) have been redacted or omitted from the thesis. When sources requests quotation checking the source is given the option of reading through quotations to verify its accuracy and that anonymity is preserved.

4.3 Data Analysis

To minimize interpretation bias a coding system was developed to analyze the collected data. In an initial coding scheme, elements were selected based on the interview protocol. After identifying promising elements from interviews to build theory upon, a new coding scheme was developed based on ambidexterity theory and timing of the transition from technology exploitation to market exploration.

Each case was then analyzed individually with relation to the new coding scheme. Relating to timing of market exploration, activities are put into a time scale relative to the clinical trial phases. Both initiation and completion timing are when possible noted down to indicate if activities overlap both within and between domains.

With relation to ambidexterity, specific indicators known from existing literature are used to rate the degree of firm ambidexterity and what type of approaches the firm utilizes to deal with ambidexterity challenges.

Finally, a cross case analysis is done to compare cases and reach an overall conclusion with relation to the propositions.

Ambidexterity coding scheme

Existing literature has identified several inter- and intra-firm indicators of ambidextrous organizations. Since the collected data contained little information about inter-firm (partners, contractors etc.) relations, intra-firm indicators are not utilized.

To determine the degree of ambidexterity in a firm, a set of intra-firm indicators are chosen from literature. The selected indicators are: balance of transactional and transfor-
national’ leadership styles, mix of ‘hierarchical and horizontal’ organizational structures, degree of ‘bottom-up, top-down and horizontal’ knowledge in-flow and levels of ‘trust, discipline, stretch and support’ firm culture (Gibson and Birkinshaw 2004).

First, the balance between transactional and transformational leadership styles is selected for particularly, as leadership ability to utilize both styles are found to have a positive impact on firm performance (M. Tushman and OReilly 1996; W. K. Smith and M. L. Tushman 2005).

Secondly, organizational structure, both formal and informal, plays a role as an indicator of how ambidextrous a firm is. The more hierarchical the more exploitation focused (Burns and Stalker 1961), while the more horizontal the more exploration focused (Duncan 1976). To be ambidextrous, a firm then has to balance between hierarchical and horizontal structures (Adler, Goldofitas, and Levine 1999; Jansen, Van Den Bosch, and Henk W Volberda 2005; Sheremata 2000).

Third, how knowledge flows between firm employees also provides an indicator of how ambidextrous a firm is. Top-down knowledge flows (Egelhoff 1991; Schulz 2003) and bottom-up data flow (Brady and Davies 2004; Sanchez and Heene 1997) supports exploitation. Horizontal knowledge (J. Galbraith 1973; Subramaniam and Venkatraman 2001; Tsai 2001) and bottom-up knowledge (Burgelman 1983) flows supports exploration. the difference between bottom-up data vs bottom-up knowledge is that data is unambiguous in structure (e.g. spreadsheet numbers) while knowledge requires interpretation and is ambiguous (e.g. the meaning of spreadsheet numbers). Ambidextrous firms should then show high and balanced levels of information flow, indicating support for both exploration and exploitation (Mom, Van den Bosch, and Henk W. Volberda 2007).

Finally, to differentiate between task partitioning approaches vs contextual approaches, notable features of contextual approaches are included in the coding scheme. According to Gibson and Birkinshaw, the notable features of contextual approaches are ‘alignment and adaptability’ across an entire business unit(Gibson and Birkinshaw 2004). To test for these, Gibson and Birkinshaw have utilized known indicators of ambidexterity such as signs of high levels of trust, discipline, stretch and support.

However, for contextual ambidexterity to be present, individual creativity and innovation has to be encouraged throughout the whole organization. Such a firmwide balance will only be possible in organizations with low power distance and high levels of individual autonomy. As such ‘power distance’ and ‘individual autonomy’ is utilized as control indicators.
5 CASE STUDY FINDINGS

Names of sources have been altered. All source names are given the same initial letter as the name given to the cases, Alpha, Beta and Gamma (e.g. Bob works in Beta, Aaron works in Alpha, etc.).

5.1 Alpha Corporation Case

Interview subjects indicate that Alpha corporation have 30 (roughly) employees and that the firm is heavily invested in R&D and new product development. Two mid-level managers (Aaron and Adam) in Alpha are interviewed. Both have extensive experience managing clinical trial processes at Alpha and at former workplaces. The firm has in total three products on the market or in phase II/III. If referring to products, they will be named chronologically as Alpha one, Alpha two and Alpha three. While no longer an early start-up firm, the firm has not yet turned profitable despite out-licensing of Alpha one generating some revenue.

The core technology of Alpha comes from a university hospital institution; the university hospital were their first pilot customer and is a major shareholder in the firm. Initial founders are scientists and medical practitioners with an background in academic or clinical work. While the university hospital is a pilot customer, extensive external funding was still needed to complete the clinical trial process of their first product, Alpha one.

The firm was created to commercialize technology developed at the university hospital for in-house treatments. As such, the firm had an advantage in that some of the R&D necessary for approval and commercialization had already been done on the Alpha one
product when the firm was started. Alpha one generates enough revenue to support further R&D but did not become an great commercial success.

According to Aaron (in hindsight), the Alpha one product had a somewhat unwieldy procedure and caused patient pain; reimbursement schemes also favor existing treatments, ensuring that potential customers (doctors/hospitals) are disincentivized to adopt the Alpha one product. The root cause for a mediocre commercial performance of Alpha one is that the potential customers are not sufficiently engaged in the new product development. Because the pilot customer had done extensive in-house testing of Alpha one the firm was overoptimistic about the procedure being transferable to a larger commercial market. Despite these issues, top management are perceived as having a market oriented attitude because they tried to address the market with the resources they had available at that time. For example, employees who were doing R&D were also acting as sales agents according to Adam:

“in early [firm start-up] phase scientists were also sales people, and at that time it was the right thing to do.” -Adam

Subsequent new product development after Alpha one has changed to become more responsive. While the core technologies remain the same, how the product is applied and how the firm perceives who the real customer/patient is has changed. This is also reflected within the firm as the founders who have remained with the company have also gone through an evolution from being scientists to becoming more market oriented, while their continued presence is considered an vital asset in balancing technology with market considerations.

**Addressing Proposition 1**

As a result of an increased market orientation, market considerations gain a lot more attention during the product development of Alpha two and Alpha three. Alpha two is extensively tested on potential patients and an innovative application mechanism has been developed to overcome the usability issues that plagued Alpha one. Aaron stresses the importance of discovering who the future patients and customers would be and the use of patient/customer feedback to improve the Alpha two product.

“ In phase IIb if you will, then you should have done this [market exploration] before phase III. And it is not easy, especially for start-ups because they do not have the right people for this at all. They are built up with only scientists and people doing clinical trials and lack the right people.” -Aaron

Alpha three targets a completely novel market segment that is distinctively different from the markets served by Alpha one and two products. Due to the novelty of the market and experiences with the mediocre profits from Alpha one, Alpha three product development also focuses on identifying and developing favorable reimbursement models and
strategic marketing towards future customers has become an integral part of the clinical trial process. Noticeably, Adam explains that by phase II the firm incorporates active marketing activities into the phase to target future customers.

“Selection of sites for phase II/III are an important strategic choice to grow the market.” -Adam

“[Marketing] is initiated in phase II by choosing test sites that could be future customers.” -Adam

Furthermore, phase III is designed to include data that have little impact on a potential clinical approval but aims to convince market and customers of Alpha three’s superiority compared with existing products.

“Phase III generates important data to convince market and customers.” - Adam

Given this, the author found support for proposition 1 (see 3.4, page 14). By the initiation of phase III, Alpha engages almost exclusively in market exploitation by incorporating future marketing elements into the clinical trial phase. Phase II also contains large elements of market exploitation (site selection), as site selection necessitates that the firm have a clearly defined customer demography. Aaron confirms this by stating that exploration should be completed before phase II ends. Thirdly, the fact that Alpha three product is targeting a novel market that have little resemblance to Alpha one and two markets implies that initiation of Alpha three market exploration must occur very early in the clinical trial process, as market knowledge from Alpha one & two cannot be directly transferred to Alpha three product development.

**Addressing Proposition 2**

As previously quoted, from the early start-up phase of Alpha, top management stressed the need for a balance between technology and market domains by making scientists act as sales agents. The continued presence of founders in top management is credited to their willingness to put effort into learning the market domain while still retaining technology domain specific knowledge.

Alpha firm structure is formally arranged in an hierarchical structure while the majority of the firm’s employees spends their time doing R&D or managing the execution of ongoing clinical trials. All activities happen within the same business unit. The responsibilities of managing each new product is delegated to cross-class project teams who operate outside the formal vertical structure. A notable feature of these project teams are that they have a large influence on decision making and that top management approval is largely a formality.

“[Project] decisions are taken in the group, subject to top management approval. Seldom have top management rejected us.” -Aaron
Cross-class team membership consists of people from all levels of the firm and represents all the components needed for a complete new product development including out-licensing specialists and sales&market strategists. Both Aaron and Adam believe that every member of the team contributes to the whole of new product development and confirms that important market discoveries and market contributions has come from people primarily engaged in technological R&D or clinical trial execution.

Top management attitudes towards project teams are characterized by high levels of trust and an simultaneous (paradoxical) 'hands-on' and 'hands-off' approach. Aaron explains that top management are among the members of each project team, but when they are actively participating in discussions they are acting more as equal members rather than as team directors.

“It is seldom, only when taking big decisions we have to lift the decision to top management. And we have dialogues going with managers individually, so it is a quite informal, not as rigid as it might sound.” -Aaron

Based on the interviews, Alpha displays many characteristics of ambidexterity such as signs of high levels of trust, discipline, stretch and support, all known to positively correlate with high levels of ambidexterity (Gibson and Birkinshaw 2004). Secondly, cross-class teams operating outside the hierarchical structure indicates either a task partitioning or contextual approach to overcoming ambidexterity challenges.

Furthermore, both of the interview subjects claim that the characteristics mentioned are an critical part of the firm’s survival and future economic success. As Adam put it:

“The [firm’s] strength is a lot of enthusiasm, drive to create and belief in the firm and the technology.” -Adam

Thus, in Alpha the author finds clear support for proposition 2 (see 3.5, page 17). The firm shows clear signs of using task partitioning or contextual ambidexterity to balance the needs between exploration vs exploitation, and furthermore that the managers themselves perceive this as an critical success factor.

Addressing Proposition 3

During the interview Aaron explains that new ideas are also generated by people outside the project management teams:

“We [firm employees] talk and collect ideas all the time on technology and the market. We have a lot of discussions and share information.” -Aaron

This is also supported by how Adam recalls the earlier times in the company:

“in early [firm start-up] phase scientists were also sales people, and at that time it was the right thing to do.” -Adam
While the question whether Alpha is currently using an contextual strategy or not is open to debate, there are indications that it previously required all employees to engage themselves in both market and technology domains. With this in mind the author finds support for proposition 3 in the early start-up phase of Alpha but cannot decisively conclude whether Alpha is still utilizing an contextual approach to overcome ambidexterity challenges.

5.2 Beta Corporation Case

Interview subjects indicates that Beta corporation have 30 (roughly) employees and that the firm is heavily invested in R&D and new product development. Three mid-level managers (Bartholomew, Benjamin, Bob) are interviewed. All are involved in current new product development projects and have extensive experience with managing or evaluating phase II/III clinical trials at former workplaces.

Core technology is an industry spin-off from a large industry corporation which at an earlier time diversified into several high-tech sectors outside its core 'big-iron' industries. As a consequence of strategic choices by the larger firm, Beta was spun off as an independent firm. The parent corporation does not retain any financial interests in Beta nor does it supply funding. Beta did not have a typical “founding team” since it had formerly been part of a large corporation, and only a very small number of employees remain since the spin-off event. None of the interview subjects have been employed by Beta prior to the spin-off event, making them non-primary sources of information on how past experiences have affected the firm.

Beta has developed a total of three products which have reached phase II/III. These will be referred to as Beta one, Beta two or Beta three. While the firm is not an early start-up, none of the products has generated any significant revenue capable of supporting further R&D.

The firm develops niche markets by identifying existing treatments that they can improve with their core technology. Beta one was out-licensed but failed in late clinical trials. Beta two has recently failed in phase II trials and the firm is waiting for the results in phase III trial for Beta three. During the interview period the results of Beta three clinical trial came back negative. While such an event will surely have some impact on the interview subjects, support for the case findings is also found in data gathered prior to this event. Given that no Beta products have reached the market the interview subjects cannot offer definitive answers to what would be the specific success factors for Beta’s new product development.

Addressing Proposition 1

All of the interview subjects have extensive knowledge and experiences with conducting clinical trials prior to joining Beta. While not being able to give first hand accounts
of Beta’s past, all of the interview subjects indicate that the firm has become more market oriented since their employment. All the interview subjects stress the importance of early market exploration and how important it is for successful commercialization of an treatment.

Based on his own experience, Bartholomew makes it clear that activities in applied research plays a critical support function to further market exploration.

“[A Bio-tech start-up] almost always underestimates what studies should be done early [to reach market]” - Bartholomew

While not conclusive, Bartholomew’s statement gives (anecdotal) support to the assumption that initiation of market exploration occurs after technology exploitation, because Bartholomew sees technology exploration as an important pre-requisite for successful market entry.

In direct relation to proposition 1, Bob takes the most extreme position by emphasizing that market exploration should ideally be initiated before initiating pre-clinical trials to ensure that there is an viable market. Benjamin explains that such a screening process have become an integral part of the firm’s new product development prior to doing any clinical trials.

“the market should be part [of the clinical trial process] all the time, but by phase II it must be part of the picture” - Benjamin

Given that all interview subjects have extensive experience with clinical trials and there is very little disagreement between the sources, the author finds support for proposition 1 (see 3.4, page 14).

**Addressing Proposition 2 & 3**

Beta firm structure is formally arranged in a hierarchical structure while the majority of the firm’s (roughly) 30 employees spends their time doing R&D and managing the execution of ongoing clinical trials. Outside this formal vertical structure, the responsibilities of managing each new product is delegated to cross-class project teams. Beta is in this aspect virtually identical with Alpha.

Project team membership consists of people from different backgrounds representing all levels of the firm. While the formal organizational structure and individual attitudes could indicate an ambidextrous organization, other crucial indicators are missing.

Two factors contributed to such an interpretation. Firstly, top management is largely absent from the daily activities within the firm and there are clear indications of a high power distance between Top Management and employees. While in theory the firm has an ‘open-door’ policy, multiple interview subjects indicate that the firm culture only accepts debates as long as it does not “rock the boat”. This indicates a lack of acceptance for divergent thinking, a crucial characteristic of exploration activities (J. G. March 1991).
“It takes unbelievably long time before a professional’s medical advice is accepted [by management]” - Bartholomew

Secondly, there are indications that decision-power is retained in top management and project teams are mainly tasked with execution, another clear indicator of an firm utilizing a ‘single focus’ approach focused on exploitation activities.

“Management has a large influence, the Top Management make all the decisions and our [project team] task is only to execute.” - Bartholomew

While interview subjects all confirm there is a need for more trust, discipline, stretch and support, on a firm level the indications are that Beta displays low levels of trust, discipline, stretch and support (Gibson and Birkintshaw 2004). The firm shows signs of following a ‘single focus’ on exploitation, while the interview candidates indicate a desire for a more balanced approach. As such, weak support is found for proposition 2 (see 3.5, page 17) but not sufficient support to conclude anything with regards to proposition 3 (see 3.5, page 17).

5.3 Gamma Corporation Case

Interview subjects indicates that Gamma corporation has 300 (roughly) employees where over 200 are employees at an in-house manufacturing unit. The interview subjects confirm that the firm is heavily invested in R&D and that new product development is the core business of the firm, despite the firm having a manufacturing business unit. Two mid-level managers (Garry and George) are interviewed. Both are involved in current new product development projects and have extensive experience with managing or evaluating phase II/III clinical trials at former workplaces.

Gamma had initially developed two non-pharmaceutical products, and later sold all rights and production capability to these products prior to engaging in pharmaceutical product development. Among its pharmaceutical products they have two products, one being marketed and the second in phase II/III. The product available on the market will be referred to as Gamma one while the new product development candidate is Gamma two. Gamma one sales generates significant revenues capable of supporting further R&D. Production of Gamma one is done in-house, while all B2C related sales, logistics and marketing is done by partners. Funding for new product development comes primarily from revenues, but the costs of late phase clinical trials are often shared with external partners.

Gamma’s core technology is a industry spin-off from the same large industry corporation as Beta’s technology. The parent corporation does not retain any financial interests in Gamma nor does it supply funding. Nor does Gamma have a typical “founding team”, and only a very small number of employees have remained since the spin-off. Neither of the interview subjects have been in Gamma from before the spin-off making them non-primary sources of information on how past experiences has affected the firm.
Unlike Beta, Gamma initially developed mass market products before switching over to becoming a pharmaceutical R&D intensive firm. Current new product development targets non-niche markets where technology-driven modifications to the firm’s original products (and raw materials) gives the new product candidates clinical benefits (making a clinical trial process necessary). While Gamma one and Gamma two are based of the same core technology, the products target different markets. Gamma one and Gamma two both target markets where there are significant levels of competition, and the firm also spends considerable R&D effort to improve manufacturing efficiency to reduce cost per unit.

An issue related to analyzing Gamma is that the firm has two business units, manufacturing and R&D. This raises the question whether Gamma could in fact utilize a structural ambidexterity approach. This possibility was discounted after analyzing interviews when it became clear that the main unit of the firm is the same as the business unit where interviews are conducted. In other words, the unit-of-analysis (business unit) is not single focused on exploration while the other unit is focused on exploitation, a characteristic of firms utilizing an structural approach.

**Addressing Proposition 1**

Both interview subjects have extensive experience with managing clinical trials from former workplaces. Overall, their view is that technology and market domain challenges overlap during the clinical trial process and that the individual phases of a clinical trial process have distinct characteristics that can be utilized to the firm’s advantage if discovered and properly executed.

For example in a phase I trial, it is possible to design the trial so that it generates important data that supports both technological improvement and market exploration. Both interview subjects stress that whether a phase I trial achieves its end-point goals or not are irrelevant with regards to the trial generating important data. The only true “failed” phase I clinical trials are those that are inconclusive.

By the end of a phase II trial, enough information is available on what technology can support in the market, permitting initiation of market exploitation activities.

“You know during the pre-clinical what market you will enter, but when you reach phase II you can perceive the magnitude of [clinical] effects, the complete picture and then you must adjust. Then you position yourself in relation to competitors or in relation to the market.” -George

Before a phase II trial is initiated, George indicates that the more commercially oriented employees will initiate market exploration and one of his roles in the phase II preparations is to ensure that such identified market possibilities are integrated into the ongoing clinical trial process.
“Then [In phase II] business development enters, because we cooperate with the purely commercial people who have been going out to ask “Where is the hole? where could we operate?”.” -George

Supporting this, George explains that the execution of any innovative market approaches can only occur until after the phase II trial has been completed.

“Before you reach phase III you have very little room to be [market] innovative, when you reach phase III you have to be innovative”. -George

Summing up the Gamma findings related to timing of market exploration: First, during pre-clinical trials the technology places limits on the potential market opportunities. Second, activities done during phase I can contribute to knowledge in both the technology and market domains. Third, market exploration and exploitation occurs simultaneously in phase II. Fourth, from the beginning of phase III the primary market activity is execution (exploitation) of (possibly innovative) market strategies. As such, the author found support for proposition 1 (see 3.4, page 14).

Addressing Proposition 2

Gamma firm structure is formally arranged in a hierarchical structure similar to Alpha and Beta. Discounting the manufacturing related employees, the majority of the firm’s employees spend their time doing R&D and managing the execution of ongoing clinical trials. Outside the formal vertical structure, the responsibilities of managing the new product development and clinical trial processes are delegated to cross-class project teams.

Similar to the other cases, cross-class team membership consists of people from all levels of the firm and representing all the components needed for a complete new product development including out-licensing specialists and sales and market strategists. The distinct feature of Gamma are the in-house manufacturing capabilities, its larger size and more stable revenues. In-house manufacturing experts are part of the project teams and their presence are credited to a need to integrate manufacturing into the clinical trial process to ensure a better balance between technology, manufacturing and market needs.

In Gamma the top-level management has been replaced multiple times, and there are indications that the former CEO had an strong transactional leadership style. The current CEO is perceived to be more balanced between transformational and transactional leadership styles. The current CEO was groomed and selected by the former CEO because the former CEO recognized a need for a more balanced leadership style.

The leadership style described by the interview subjects are that leadership is neither ‘hands-on’ or ‘hands-off” in style. The leadership does make important decisions but displays trust in subordinates, while still expecting to be kept informed.

“[Leadership] have been very little authoritarian but they set goals and expect their demands to be met.” -George
Paradoxical thinking is a clear indicator of ambidexterity traits, and the above statement has somewhat of a paradoxical nature. How could someone not be engaged in paradoxical thinking when claiming that leadership is little authoritarian while simultaneously demanding a goal achievement?

When looking at the control variables, the subjects indicate that when top management gives support for a project, it is given unconditionally and decision power is delegated to the project teams. Both interview subjects emphasize that the firm also has very low power distances.

“We have been very lucky because when they [Top Management] have said they support us they have been 100% behind that decision.” -George

“With regards to drug development, a lot of responsibilities have been placed downwards.” -Garry

“ We have a flat structure, and there is a very short distance from whomever-they-might-be in a project to the CEO.” -George

“We have a formal hierarchy, but in practice every door is open.” -Garry

With regards to how information is flowing within the organization, information is expected to flow both within the project teams and within the firm regardless of any hierarchical status. Flow of information and communication at all levels is expected to occur informally and it is the responsibility of every project team members to give full disclosure before project meetings.

“Most communication and information flow happens in the daily work.” - Garry

“Information should not be presented at meetings, meetings should be used to make decisions.” -Garry

With regards to communication and knowledge transfer with top management, the emphasis is that information flow has to be both bottom-up and top-down for the firm to succeed. As George put it:

“It is important that signals from R&D reach the leaders so that they can understand what is happening. It is important that leaders have an understanding of what the potential can be while simultaneously understanding the risks.”
-George

Lastly, one important success factor for clinical trial new product development is the necessity of horizontal communication and individual discretionary decision on when to engage others to reach a decision.
“It is vital that people have a good internal network, knows whom they should talk to and when they should involve the right people when making an decision.” -Garry

The above statements indicates that Gamma intra-firm relations displays high levels of trust, discipline, stretch and support (Gibson and Birkinshaw 2004), permitting the possibility of the firm utilizing a balanced approach to overcome ambidexterity challenges. Furthermore, top management traits are present that have an positive effect on firm ability to overcome ambidexterity challenges. Based on the interview subjects responses, the author found strong support for proposition 2 (see 3.5, page 17).

Addressing Proposition 3

A notable element of Gamma is also that the interview subjects are intrinsically motivated rather than extrinsically motivated. For example, while the firm certainly has bonuses and financial incentives, it is not raised as a point when discussing their motivation.

“This is a knowledge intensive firm, and the most motivating [incentive] we can get is the nuts we manage to crack.” -Garry

Given that low power distance and high levels of autonomy have already been established for Gamma, the only remaining indicator to separate contextual from task partitioning would be that every employee contributes to both exploration and exploitation activities.

“We are encouraged to be creative and innovative every one of us.” -Garry

Throughout the interviews both subjects gave the impression that the major success factors in the current new clinical trial product development processes are the combination of early market orientation with a firm environment where every employee somehow contributes to both exploration and exploitation. Based on the interview subjects responses, the author found support for proposition 3 (see 3.5, page 17).

5.4 Cross Case Analysis

Before dealing with any cross-case patterns, there are important caveats to keep in mind with regards to analyzing some of the cases. In the case of Beta, the fact that all the firm’s products have failed in late stages of clinical trials cannot be interpreted as ’proof’ for any proposition, since the industry wide failure rate of 9% cannot be explained solely by late market timing or a firm’s approach to ambidexterity (or lack thereof). Thus, at best, only correlation can be established. In the case of Gamma, the success of the firm leading to the firm no longer fulfilling the typical start-up criteria are another side of the same issue with regards to Beta. Correct cross-case analysis cannot directly use the success of Gamma as a ’proof’ for any propositions.
Addressing Proposition 1

Based on each case and interview statements it is possible to construct a time-line for each firm (see figure 8) on when different activities are initiated and completed. The overall data indicates **strong support for Proposition 1**. *The earlier a pharmaceutical start-up firm engages in market exploration, the more likely a clinical trial process leads to commercial success.*

![Activity timing chart in clinical trial process](image)

In all cases, market exploration is initiated at the latest in the pre-clinical trial stage and in all the cases early timing of market exploration is stressed as an critical success factor. While Alpha initiates market exploration activities somewhat later than the other two cases, Alpha employees indicates that one of the goals of the firm is to in the future be able to initiate market exploration earlier. The findings from the more established Gamma supports this as Gamma employees made it clear that the firm has taken steps to initiate market exploration earlier based on prior experiences.

Addressing Proposition 2 & 3

Based on the table of ambidexterity indicators (see table 1) used for data analysis and the individual cases a cross-case table is developed (see table 2). A firm rating of ++ or +++ is assigned to each case when possible. Based on existing literature, ability to use simultaneous approaches to ambidexterity challenges can only be said to be present in the cases where indicators within the same group are fairly balanced and rated medium to high (++)

\[1\]

This does not apply to the control variables. Low power distance(+) and high individual autonomy(+++) are conductive to approaches that balanced ambidexterity.
Table 2: Cross-case comparison of ambidexterity indicators

<table>
<thead>
<tr>
<th>Ambidexterity Indicators</th>
<th>Rating (+/++/+++</th>
<th>Alpha</th>
<th>Beta</th>
<th>Gamma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leadership</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transactional</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Transformational</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Org. Structure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hierarchical</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Horizontal</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Information flows</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Top-down knowledge</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Bottom-up data</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Bottom-up knowledge</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Horizontal knowledge</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Contextual Org.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>trust</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>discipline</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>stretch</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>support</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Control variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power distance</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Individual autonomy</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
</tbody>
</table>

The general impression of Alpha and Gamma is that they are more capable, compared to Beta, at discovering market opportunities and utilizing them. As both Alpha and Gamma score higher on indicators of simultaneous ambidexterity the overall data indicates support for Proposition 2, Utilizing a task partitioning or contextual approach positively moderates the likelihood of a clinical trial process leading to a commercial success for pharmaceutical start-ups.

Looking at only the indicators of ambidexterity, both Alpha and Gamma score medium or high. This indicates that both firms are ambidextrous, but this alone is not sufficient to conclude that the firms are utilizing simultaneous approach such as task partitioning or contextual approaches.

To build the argument that Alpha and Gamma are utilizing simultaneous approaches to solve ambidexterity challenges, exploration and exploitation activities in each of the domains have to overlap, implying that the firms has to balance two opposing activities at the same time. In the activity timing chart (see figure 8), it is clear that both firms are simultaneously conducting exploration and exploitation activities within each respective domains.

In the case of Gamma this is even more notable as the firm during phase 1 is doing all four different types of activities at the same time. This can be explained by the fact that Gamma has left the early start-up stage and now has the resources to pursue simultaneous activities within both domains at the same time. Another notable observation from the activity timing chart (see figure 8) in the case of Beta is that market exploration and market exploitation activities does not occur simultaneously. This strengthens the argument that Beta scores low on approaches to ambidexterity.
In relation to proposition 3, the overall data indicates weak support for Proposition 3, Utilizing a contextual approach has a greater positive moderating effect than task partitioning approaches has on the likelihood of a clinical trial process leading to a commercial success.

While Alpha and Gamma cases score high on contextual approaches and both fulfil the control variables (lower power distance and high individual autonomy), only Alpha strictly fulfils the case selection criteria of still being a start-up firm.

While analyzing Gamma individually gave support for proposition 3, the combination of Gamma’s size and the fact that the interview subjects had not been in the firm while it was still a start-up, makes it more difficult to argue that Gamma did utilize contextual approaches when it was more resource constrained.

6 Discussion

There has been little research done on innovation and the forces driving new product development in pharmaceutical industries. The only comprehensive publication on innovation in pharmaceutical companies was done by Takuji Hara in 2003. The clinical trial process that bio-tech and pharmaceutical industries have to adhere to also creates an environment where the industry language is hard to comprehend for people lacking an background in natural sciences.

The author contributes to the existing literature on innovation by investigating how existing theories on antecedents of ambidexterity applies to the new product development (NPD) process in pharmaceutical industries. This NPD process called a clinical trial process is shown to be an useful proxy for gauging start-up firm success within pharmaceutical industries, as all the vital element of NPD success (or failure) are addressed within a clinical trials process. For example, after successfully completing a clinical trial process and gaining marketing approval, products are only assumed to have an 80% chance of being a commercial success. However, bear in mind that in most other industries an 80% chance of commercial success after product launch would be considered a dream-come-true.

The reason for this peculiarity is that the pharmaceutical industries lack many of the features of more complex industries; for example the long product development cycles give firms ample time to investigate and formulate strategies in comparison with more fast-paced industries. Another simplifying feature of intra-firm relations is an almost complete lack of competition. This makes the pharmaceutical industries almost ideal candidates for investigation on how “soft” values such as organizational culture affects firm success without being distorted by competitive market forces.

However, while pharmaceutical industries face little competitive forces, new product development has to be tailored to a specific patient group and the needs of that group has to be intimately understood in order for NPD to success. Secondly, technology plays a
very important role, as it defines what is permissible. However, the role of technology should not be overstated according to Hara (Hara 2003). Hara concludes that the true limiting factor appears to be how well possible market applications are imagined and created rather than them being a discovery of a pre-existing opportunity.

6.1 Theoretical Implications

Based on an deductive qualitative method, two important propositions are developed. Firstly, that while the new product development cycle can take more than a decade, initiation of market oriented activities should be done ‘the earlier the better’ for successful new product development. Secondly, that while pharmaceutical start-ups are largely virtual, outsourcing does not alleviate the need for balanced approaches to ambidexterity challenges. In fact, the extensive outsourcing makes a balanced approach more important, as the pharmaceutical firm has to maintain a holistic view throughout the whole of the clinical trial process to ensure that all parts continually contribute to the whole.

Timing of clinical trials

While technology exploration seldom occurs simultaneously with market exploitation, technology exploitation and market exploration largely overlap (see figure 8). This somewhat contradicts Lavie and Rosenkopf’s (Lavie and Rosenkopf 2006) conclusion that firms tend to balance exploration in one domain with exploitation in another domain. However, Lavie and Rosenkopf only test their hypotheses on intra-firm domains, not inter-firm domains. Secondly, Lavie and Rosenkopf investigates the software industries where competitive forces are significantly stronger and strongly impact alliance formation. The strong support found for proposition 1 indicates that market exploration could occur simultaneously with technology exploration when competitive forces are largely absent. As a consequence, while Lavie and Rosenkopf theoretical framework is transferable their findings cannot be assumed to be directly transferred to inter-firm domains or to other industries.

Approaches to Ambidexterity

The conflicting demands between technology and market are generally accepted in literature, but little research has been done to identify how technology vs market domain knowledge interacts with the learning behavior that support exploration vs exploitation. Lavie and Rosenkopf’s domain specific ambidexterity is a promising framework for investigating and identifying critical steps in a clinical trial process.

By identifying indicators of ambidexterity and differentiation between technology vs market domains, the critical step for start-up firms is identified to be in the moment when start-up firms transition from technology focus to market focus. While this is not novel
knowledge, showing that it involves a transition from technology exploitation to market exploration provides novel insight. While qualitative deductive research cannot give definitive proof or provide generalizations, it indicates that there are multiple modes of failure when attempting to overcome the “double learning curve” challenge. Often a lack of market orientation have been cited as a cause of failure for technology start-ups, but when discussing how market oriented a firm is, the balance between market exploration and exploitation can play an equally important role. For example, a firm can be interpreted as ‘highly market oriented’ but in reality be low on market exploration, implying that they will not be able to discover (or create) novel and more profitable market opportunities.

6.2 Practical Implications

For a pharmaceutical firm, the decision on when to initiate market oriented activities is paramount. The initial stages of new product development is often technology driven, but even before clinical trials are initiated a patient population needs to be defined. While established firms have prior experience with how the market interacts with their core technologies, start-up firms would have no such experience.

Given that pharmaceutical start-up firms are largely virtual, the lack of spare resources in both the managerial and financial realms makes an efficient utilization of existing resources for extended periods of time critical for firm survival.

Early Timing and The clinical trial process

Cost of running a clinical trial process are high and are expected to rise due to multiple factors. The industry perception is that some major causes are a lack of “low hanging fruits” and tighter regulatory requirements. While often cited by sources, there are also indications that this is not the whole picture.

One identified fundamental issue is the heterogeneity (non-uniform distribution) of the patient population. Population heterogeneity impacts each individual phase by introducing uncertainties related to the outcome, because the hidden variables in the sample selection strongly affects the statistical results. In the larger picture, the heterogeneity of the population introduces market uncertainties with regards to whom and where to market a new product candidate.

The case data indicated that the early stages of a clinical trial process does not leave much room for market innovation, nor does late stages leave room for technological product innovation. As a consequence of the population heterogeneity and a tight regulated clinical trial process, the more innovative a new product candidate is the more important early market exploration and the need for a balanced approach to ambidexterity became.

Secondly, the more technologically radical a product, the more heterogeneity would affect the outcome of a clinical trial process. The more radical the new application, the less value prior experience in existing markets has. The implication is that while ’the
earlier the better’ is correct with regards to the timing of market exploration, the more technologically innovative a new product candidate is, the more difficult and critical it would be to initiate early market exploration and to maintain a balanced approach to ambidexterity.

**Approaches to ambidexterity**

If firms do not simultaneously pursue ambidexterity within and between domains, they will not be able to fully utilize the feedback generated between the different exploration and exploitation activities.

Argyris’s (Argyris and Herbane 2005) ‘double loop learning’ (that supports exploration) is disruptive in nature as it calls in question the presumptions and assumptions that existing knowledge build upon. If exploration and exploitation activities do not occur simultaneously, it is less likely that the feedback generated from double loop learning would have a significant impact on subsequent exploitation activities. I.e. by avoiding simultaneous approaches to ambidexterity, a firm risks investing significant resources on “barking up the wrong tree” and having to backtrack at a later stage.

However, when pursuing any simultaneous approaches the difficulties of evaluating the feedback will rise because it involves evaluating information flows that require both single loop and double loop learning. Nor does having a organizational structure that mixes hierarchical with horizontal structures guarantee an ambidextrous capable firm. For a firm to achieve ambidexterity and fully utilize the creativity and imagination of its employees, there has to be a strong goal alignment combined with individual adaptability throughout the firm.

**6.3 Limitations**

The notable limitation of this thesis is that the results are interpreted solely based on semi-structured interviews. Case study best practice recommends the utilization of triangulation such as multiple levels of investigation to ensure that the findings are as reliable as possible. According to Yin (R. K. Yin 2008; R. K. Yin 1981), mixing qualitative methods with quantitative methods could aid in triangulation as multiple methods converging on the same propositions strengthen them. Additionally, Pettigrew (Pettigrew 1990) recommends utilization of multiple investigators to interpret qualitative data, while this thesis is written by a single author.

Besides the methodological limitations, in hindsight one of the selected cases (Gamma) does not fully fulfill the sample selection criteria. However, the generated propositions does not rest their sole argument on this single case. Secondly, while such a source cannot be used as the single support for a proposition, it is a collaborating source of information on issues in clinical trial process that more established firms share with start-up firms.
6.4 Future Research

**Empirical Testing of Domain Specific Ambidexterity**

This thesis addresses many of the limitations and future research suggestions given by Lavie and Rosenkopf (Lavie and Rosenkopf 2006) by investigating the internal domains in a non-software industry.

However, as this thesis is qualitative in nature, what remains to do would be an empirical study of internal domains in a non-software industry. Given that competitive market forces are far weaker in pharmaceutical industries, an empirical study building upon pharmaceutical R&D heavy firms and/or start-ups can be especially fruitful at building up a sound empirical basis for domain-specific ambidexterity.

**Investigate Learning Feedback in Pharmaceutical Firms**

While the Technology vs Market domains are identified in this research, other options for demarcation between domains exist in literature. Hara (Hara 2003) identifies four different distinct areas (shaping of the compound, shaping of the market etc.) in clinical trial processes that all have complex feedback loops within and between them. Existing literature on ambidexterity has shown that exploration and exploitation are differentiated by ‘single loop’ vs ‘double loop’ learning (Argyris and Herbane 2005). Given that some pharmaceutical firms have been shown to utilize approaches to ambidexterity, it can be worthwhile to investigate closer the nature of the feedback loops described by Hara and try to determine where such feedback loops intersect the areas suggested by Hara.

**Applying Penrose’s Managerial Resource Limitations to Exploration**

While not part of the theoretical framework for this thesis, there is one finding in the source data that can apply to the research streams on Resource based view (RBV) and the seminal work by Penrose on ‘The Growth of The Firm’ (Penrose 1995) that is credited for initiating the RBV.

In 1955 (republished in 1995), Penrose hypothesized that lack of spare managerial resource was the limiting factor for firm growth. This is because the smaller a firm, the less spare resources (time, mental effort) individual managers have to imagine and plan for the future. A core element of Penrose’s work is that spare managerial resources limits the rate of consumption and efficiency of consumption of other resources. However, the RBV has to some extent ignored Penrose’s argument that managerial resources are rate limiting while drawing on her core idea of resource limitations being a critical factor for firm growth. In RBV, resources (both tangible and intangible) are classified and prioritized on how rare or imitable they are, where hard-to-copy and rare resources are valued highly.

However, RBV has as a result been criticized for being tautological, i.e. rare is rare, imitable is imitable. While conducting interviews, the sources indicate that in the pharmaceutical industries financial resources mainly limit exploitation activities, while explo-
ration activities are limited by managerial resources. This implies a possibility to reconcile Penrose with the RBV by drawing on ambidexterity theories to show that Penrose was addressing resources limitations on exploration activities while RBV primarily addresses resources limitations on exploitation activities.

7 Conclusion

The author drew on a natural science background to investigate how a clinical trial process affects innovation in pharmaceutical start-up firms. A key assumption is that pharmaceutical start-ups must simultaneously pursue exploration and exploitation in different domains. The identified domains are technology vs market, known from existing literature to have conflicting demands. Key findings are that early initiation of exploration in the market domain is critical to success in new product development for pharmaceutical firms. The more innovative a product, the more important early market exploration becomes. Pursuit of balanced exploration and exploitation is also found to positively moderate economic success in the investigated cases.

Acknowledgments

I would like to first thank my Supervisor Birthe Soppe for her patience when ideas and concepts are generated by my head faster than I can articulate them. I would also like to thank my friends Hillary Kyler, Tuva Selmer and Kristian Løvås for keeping me remarkably sane and grounded in the world outside academia. Other contributors to the author’s sanity shall remain anonymous but not forgiven.


Hay, Michael et al. (2011). “BIO / BioMedTracker Clinical Trial Success Rates Study”.


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Appendix
Inquiry about participating in research (master thesis) on clinical trial innovation

Dear Sir or Madam,

My name is Heikki Sørurn and I am currently working on my master thesis in Entrepreneurship and Innovation at Oslo University (UiO), with a topic related to biomedical industry and innovation. Besides an interest in Innovation and Entrepreneurship I have a Bachelor in Chemistry from the University of Oslo with a focus on quantum chemistry and nano-material synthesis.

Research background & goals

Succeeding in clinical trials is an important market barrier for life science startup companies. While there is a lot of medical literature written about designing, conducting and analyzing clinical trials, surprisingly little research is available on clinical trial design in the context of business strategy and business development.

I am looking for interview partners for my master thesis and I hope some of your firm’s leaders or founders could participate as subjects for my thesis in Success and failure of innovative clinical trial design among life science companies.

With your company’s permission, it would entail individual interviews with up to 3 relevant managers for roughly 1 hour each. Specifically, the research involve face to face interviews with managers who were involved in decisions on clinical trials in your company. I can also mention that the founder of Bionorpharma ASA Birger Sørensen have agreed to act as industry reference. ¹

Result for your company

The final thesis will contain an executive summary section written specifically for business oriented readers, and all participants can get a copy of the final thesis. The practical reward for your participation is two-fold:

- You could get some (anonymized) insight in how other life science startup companies think and reason with regards to their success factors in clinical trial design.
- Insight in how life science companies innovate in the larger context of research on innovation and entrepreneurship.

Ethical considerations

The research is done in accordance with the University of Oslo rules for master thesis work and the accepted norms of ethical conduct for academic research. For you as a potential participant the most relevant implications are:

- All participants must give explicit consent and be informed of the research topic and its goals. Consent can be withdrawn at any time for any reason prior to completion (15 May 2013).
- The content of a thesis is made public 2 years after its completion. Though, the author can withhold electronic publication indefinitely.

¹ +47 404 07 565 / bs@bionorpharma.com / bsoren@online.no
• The identity of all participants and participating organisations will be kept confidential (anonymized). This applies both in the final delivery and in any gathered data that could be made available to others in any form.

The supervisor for this thesis is Dr. Birthe Soppe ² Assistant Professor at Centre of Entrepreneurship (SFE), UiO.

Sincerely,

Heikki Sørum

²+47 22 84 09 19/ birthe.soppe@sfe.uio.no / Senter for entreprenørskap, Postboks 1169 Blindern, 0318 Oslo
1 Research question

RQ: “What determine the success or failure of clinical trials for entrepreneurial life science companies?”

2 Concepts

Market orientation was defined as “the capability to generate, disseminate, and respond to intelligence pertaining to current and future customers” (Kohli & Jaworski, 1990)

“Transactional leaders focus on making incremental improvements and making the best use of existing process.” (Jansen et al., 2009)

“Leaders who are transformational encourage “out of the box thinking”, information sharing and question assumptions” (Jansen et al., 2009)

“Red oceans represent to all the industries in existence today – the known market space. In the red oceans, industry boundaries are defined and accepted, and the competitive rules of the game are known. Here companies try to outperform their rivals to grab a greater share of product or service demand. As the market space gets crowded, prospects for profits and growth are reduced. Products become commodities or niche, and cutthroat competition turns the ocean bloody; hence, the term red oceans.” - W.Chan Kim and Renee Mauborgne. INSEAD. 2005.

“Blue oceans, in contrast, denote all the industries not in existence today – the unknown market space, untainted by competition. In blue oceans, demand is created rather than fought over. There is ample opportunity for growth that is both profitable and rapid. In blue oceans, competition is irrelevant because the rules of the game are waiting to be set. Blue ocean is an analogy to describe the wider, deeper potential of market space that is not yet explored.” - W.Chan Kim and Renee Mauborgne. INSEAD. 2005.

3 Study questions

General background

1. How many clinical trials have you done?
2. How did they go and how did you evaluate them?
3 STUDY QUESTIONS

3. What kind of products was it and what was the intended patient group(s)?
4. What/who were the individuals that was involved in decision making?
5. How many full-time employees does the firm have?
6. How many of the company founders are still in top management positions?

**Market Orientation**

1. Do you consider market uncertainty when deciding on clinical trial goals?  
2. Does the firm’s segmentation aim for a narrow or wide patient population? 
3. Does the firm try to define an initial small, narrow and exclusive market segment? 
4. How does your firm determine the market demand? (Responsive, dialogue with current and future customers) 
5. And when does market demand considerations enter the picture in clinical trial design? 
6. Does the firm experience a lot of competition? 
7. Does the behavior of competitors affect the design of clinical trials? 

**Leadership and teamwork**

1. Are the major business related decision in clinical trial design done by teams or by single individuals? 
2. Are the firm leadership mainly transactional or transformational? 
3. Does the leadership have an ability to change leadership style? 
4. Are the relevant (to clinical trial design) teams mainly from the same background (intra-disciplinary) or are they from diverse backgrounds (cross-class)? 
5. What are the biggest resource limitations for the firm? 
6. Does non-business development people generate ideas for and participate actively in exploring new markets? 

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1 Knightian uncertainty
2 Niche vs mass market
3 Blue ocean vs red ocean
4 Dynamic Market orientation
5 High or low market orientation
6 Competitive market orientation
7 Impact of competitive behavior
8 Team vs individual
9 Leadership style
10 Combining transactional transformational
11 Team dexterity
12 RBV vs Penrose
13 Contextual ambidexterity
3 STUDY QUESTIONS

Commercial focus and timeframe

1. What is the impact of the founders vision and market perceptions on clinical trial design? 14
2. Does the founders vision/perceptions last long enough to affect phase II or III trials? 15
3. Does/Did the founders have a clear commercial vision when they are/were in charge? 16
4. What is the timeframe from decision on a clinical trial design until it is possible to evaluate if it was correct or not (feedback cycle)? 17
5. Is the only focus of the firm technology innovation, or do they also emphasize some business (process) innovation? 18
6. Is the commercial vision or market clearly defined from the beginning or does it emerge as a consequence of results from clinical trials? 19

14Founder effect
15Founder effect impact
16Founder vision
17Iterative process or failure-is-not-an-option
18Business exploration
19Exploitation vs exploration