



Shareholder returns and the exploration–exploitation dilemma: R&D announcements by biotechnology firms

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Available online 12 April 2007

Abstract

We explore a financial returns dimension of the exploration–exploitation dilemma. Using 1277 R&D announcements by 178 listed bio-pharmaceutical firms, we examine whether investors are myopic along the continuum of exploration (patenting and preclinical trials) to exploitation (human clinical trials and NDA). We find that investors respond positively at every stage, but there are differences between small and large firms. For small firms exploration is favored, provided it is focused. For large firms, there is value in both exploration and exploitation. Projects which are part of an alliance are no more likely to generate abnormal returns. Policy implications are discussed.

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Keywords: R&D; Knowledge based view; Financial performance; Event study; Alliances

1. Introduction

A key challenge facing human therapeutics biotechnology firms is how to bridge the gap in both time and resources between discovery of a compound and earnings generated by sale of approved drugs. Recent data indicate that the time taken for a drug to move through clinical trials and the process of Food and Drug Administration (FDA) approval is now 8.5 years (Tufts, 2005), with the discovery phase estimated to be a further 2–5 years (DiMasi et al., 2003). The out-of-pocket cost of taking a drug through to FDA marketing approval is estimated to be US\$ 403 million, inclusive of the cost of drugs that fail to make it through to the end of clinical development (DiMasi et al., 2003). There are three primary mechanisms by which this gap is bridged: pub-

lic funding of research (Hyytinen and Toivanen, 2005); private capital in the form of venture funding or stock market listing; and revenue and cost sharing derived from inter-organisational alliances with traditional pharmaceutical firms (Rothaermel, 2001). Between 1994 and December 2006 it is estimated that the broad classification of biotechnology firms operating in Europe and North America have raised US\$ 194 billions in capital and long-term debt, of which about a third was raised from initial public offering and follow-on offerings (Biocentury, 2007).

This paper focuses upon public-quoted entrepreneurial bio-pharmaceutical firms listed on NASDAQ and European stock exchanges. Listing provides access to capital, in addition to an exit source for venture financiers. The creation of NASDAQ in the US and changes in stock market listing rules in several European countries in the 1990s have made it possible for small (often loss-making) biotechnology firms to quote directly upon a stock exchange and thus gain access to sources of capital and innovation incentives which were

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not available earlier (Coriat and Orsi, 2002; McNamara et al., 2000).

It has been suggested in the press and even in the academic literature that stock market investor-shareholders over-emphasize short-term earnings at the cost of longer term R&D (see Tylecote and Ramirez, 2006, for a review). This bias against long-term investment in research in, or exploration of, new technologies in favour of exploitation of a firm's current knowledge has been postulated by March (1991). If such a bias exists, it means that early stage research is disadvantaged in raising capital from the stock market. This has important policy implications.

March's (1991) theorizing that, due in part to more positive short-term returns, exploitation may drive out exploration has received mixed empirical support. Chan et al. (2001) undertook a study of all domestic firms quoted on the NYSE, AMEX and NASDAQ stock exchanges from 1975 to 1995 and found that the historic performance of firms who invested heavily in R&D did not outperform those that did not, suggesting that exploration is not necessarily associated with inferior performance. However, Hoang and Rothaermel (2006) found that the ultimate success of an alliance project is lower when initiated during the exploration stage of R&D; while, more seriously, Rothaermel (2001) found that exploitation alliances have a positive impact upon a pharmaceutical firm's new product development success, whereas exploration alliances do not. The skewed positive financial impact of exploitation over exploration activities is further evidenced in increased accounting returns generated by new product launches (Bayus et al., 2003) and also in shareholder returns (Chaney et al., 1991; Chen et al., 2002). When combined, these studies lend some support to the idea that financial returns from exploitation activities are more certain and more positive than those from exploration.

Whilst the exploration–exploitation dilemma is typically presented as dichotomous, it is clear that many writers see subtle distinctions occurring along this continuum. For example, Levinthal and March see a different valuation between “use” and “development” (1993: 105). Following the argument that exploitation drives out exploration due to clearer, more temporally proximate and larger financial feedback, the same may apply for development and use. Use activities are less uncertain in outcome than development activities and so may generate higher returns.

The theoretic perspectives of Levinthal and March (1993) are often cited in the literature; however most studies only explore the basic dichotomy between exploration and exploitation. Few studies explore the financial

impact of the micro stages that occur within each of these activities. Unpicking the micro stages may well shed light on why previous studies have been ambiguous. This paper uses the public nature of the bio-pharmaceutical industry's R&D process to explore the financial response of shareholders to announcements of positive news along six micro stages of the exploration–exploitation continuum. We classify the first two of these micro stages, namely patenting and preclinical trials, as exploration activities. We classify the remaining four micro stages as exploitation activities, namely the three phases of human clinical trials (phase 1, 2 and 3 trials) and the New Drug Application (NDA) regulatory approval process. In this industry there is a clear validation process supported by regulated bodies for each of these six micro stages of the exploration–exploitation process.

We go further than testing for a general bias against exploration; we also look for a bias against smaller firms undertaking such work. Some argue that small firms are not suited to undertake risky R&D requiring substantial knowledge and financial resources. The lack of scale and scope in smaller firms may cause them to be less efficient than larger firms in the drug R&D process (DiMasi et al., 1995). However, small firms may have a comparative advantage in early stage R&D because they are nimble and flexible (Powell, 1998).

The paper begins by exploring these arguments in some detail from a theory perspective. We then examine empirically how investor-shareholders value R&D investments in bio-pharmaceutical firms' R&D process. Our data set contains information on 1227 announcements of the initiation and progress of stages of R&D projects by 178 entrepreneurial bio-pharmaceutical firms listed on US and European stock markets between 1996 and 2003. It provides encouraging evidence that the typical investor in stock markets is not so myopic as to ignore the value potential of exploration and that they see the value of smaller firms undertaking early stage work. We consider the implications of our findings for the strategies of small and large firms. We also comment on the value of institutional policies that can be introduced to assist firms in their access to capital from stock markets.

2. Theory and hypothesis development

2.1. Exploration–exploitation theory

It was March (1991) who explicitly discussed and classified managerial search behavior on an exploration–exploitation continuum. In his modeling, he makes the claim that managers will be biased against exploratory search because “[t]he certainty, speed,

proximity, and clarity of feedback ties exploitation to its consequences more quickly and precisely than is the case with exploration. The story is told in many forms. Basic research has less certain outcomes, longer time horizons and more diffuse effects than further development of existing ones.” (March, 1991: 73). A tension between exploration and exploitation exists because “*exploitation generates clearer, earlier and closer feedback than exploration. It corrects itself sooner and yields more positive returns in the near term. As a result, the primary challenge to sustaining an optimal mix of exploration and exploitation is the tendency of rapid learners and successful firms to reduce the resources allocated to exploration.*” (Levinthal and March, 1993: 107).

From early on in the debate, writers have seen subtle distinctions occurring along the exploration–exploitation continuum. For example, Levinthal and March suggest that exploitation has two distinct phases, namely “use and development of things already known” (1993: 105). “Development” is the expansion of the firm’s current stock of knowledge, whereas “use” is the appropriation of economic returns of the current stock of knowledge. Following the argument that exploitation drives out exploration due to clearer, more temporally proximate, and greater financial feedback, the same argument may apply for development and use. Use activities are more certain in outcome than development activities, being closer to the market in terms of gaining a financial reward. This means that within exploitation phases, returns may become larger as the firm progresses from the beginning of the exploitation-development phase to its use phase.

2.2. *Prior studies*

The theoretic perspectives of Levinthal and March (1993) are often cited in the literature; however most studies only explore this concept as a bi-modal dichotomy between exploration and exploitation. Few if any studies explore the financial impact of the micro stages that occur within each of these activities. The basic work on the tension between exploration and exploitation appears in a variety of contexts, such as the role of alliances in new product development (Holmqvist, 2004; Rothaermel and Deeds, 2004), managerial processes and new business project effectiveness (McGrath, 2001), the growth of the firm (Lee et al., 2003), knowledge flows in multi-divisional firms (Schulz, 2001), performance in rugged competitive landscapes (Gavetti and Levinthal, 2000) and organizational renewal (Daneels, 2002). The evidence is generally in favor of all activities being important, but of exploitation being more valued.

The nature of the evidence that is used varies. Some writers use the structure of accounting returns to support the claim that exploitation is more financially rewarding (Bayus et al., 2003; Rothaermel, 2001). However, there are difficulties in using accounting returns. Broadly speaking accounting standards in the US and Europe require that R&D costs be expensed in the profit and loss account when they are incurred, rather than amortized over a longer period as a balance sheet asset (Khadaroo and Shaikh, 2003). This means that short-term accounting earnings will be depressed when there is investment in long-term R&D.

Using event study methods which look at investor reactions to announcements avoids this problem. Event studies isolate the value that is created by the incremental investment in R&D well before the revenues are generated. Some event studies indicate that the announcement of positive news about exploitation events generate greater positive abnormal returns for shareholders than exploration events (Kelm et al., 1995; Narayanan et al., 2000).

Like many other researchers we use event study methodologies to explore our data. The matter is not just one of empirical choice; there are theory issues at stake too. Event studies factor out general market effects to focus on firm effects (for more details see MacKinlay, 1997). Event studies rely heavily on signalling theory to draw a connection between firm activities and firm valuations. Signalling theory argues that investor-shareholders react to management communications about the ongoing activities of the firm (Alchian and Demetz, 1972; Jensen and Meckling, 1976; Littler, 2006). These signals relate to the start and end points of major strategic activities, such as R&D, and to on-going information about incremental progress such as product testing. Few announcements come as a complete surprise to shareholders: most contain information that results in an adjustment of shareholders’ expectations about the future performance of the firm (Narayanan et al., 2000). When management chooses to make a disclosure, say of its intention to undertake preclinical trials or the outcome of a previously announced preclinical trial project, shareholders use this information to incrementally adjust their expectations of the future earnings of the firm. This is ultimately reflected in their decision to hold, sell, or buy the stock of the bio-pharmaceutical firm.

2.3. *Pattern and shape of exploration–exploitation returns in bio-pharmaceuticals*

Our approach is to unpick in a fine grained manner the new product development process in bio-

pharmaceuticals as a way to break down and explore stock market responses to the exploration–exploitation continuum. We use incremental announcements of progress in the R&D process to provide a more fine-grained analysis than that offered by previous studies. To create this fine-grained approach, we focus upon six important micro stages within this industry's R&D process. The first micro stage is the award of a patent. The second micro stage is preclinical trials when the medicinal potential of the compound is assessed. The next three micro stages are discussed together and cover when the compound is being developed through the three phases of human clinical trials (phases 1, 2, and 3). The final micro stage is submission and acceptance of the NDA to regulators who grant marketing approval for the drug to be sold legally. Government bodies carefully regulate each of these stages. These six micro stages are largely linear with activity in one stage building on outcomes from all prior stages. Prior literature has characterized the early stages of this process (namely, patenting and preclinical trials) as akin to exploration and the final stages (namely, human clinical trials and NDA) as akin to exploitation (DiMasi, 1995; DiMasi et al., 2003; Flieger, 1995; Rothaermel and Deeds, 2004: 209–210). Prior literature has strongly argued that each stage represents definable progress for the R&D process.

We expect that positive news from all six micro stages will generate positive abnormal returns, in part because of the strong appropriation and regulatory regimes in which such invention takes place. This gives shareholders confidence that in the event of technical success a share of future accounting returns can be secured due to patent ownership (Coriat and Orsi, 2002). The reliability of the information announced on progress in both preclinical and clinical trials can be assessed in a structured manner within the context of stock exchange rules on forward looking statements, the technical rules of drug regulatory authorities and the professional practices and norms of the natural sciences.

Hypothesis 1. Announcements of new positive news regarding commencement or progress in any of the six stages of the bio-pharmaceutical R&D process will generate positive abnormal returns.

We now say a little more about the drug R&D process and its probabilities of success for the benefit of those who do not know the industry. The first key stage is the process of drug discovery to identify a promising drug candidate from the laboratory, including the patenting of this compound. The probabilities of success at this stage are low. However, the issuance of a patent is important

because it enables the firm to have the option of negotiating R&D and commercialization deals with collaborative partners in a more secure long-term appropriation regime (Cohen et al., 2002), and it also signals to the financial community the novelty and promise of their exploration activities (Niosi, 2003). The probability of a compound entering drug discovery making it through this stage to eventual market approval is estimated to be as low as 1 in 10,000 or 0.01% (Pharmaceutical Research and Manufacturers of America, PhRMA, 2007). The second key stage is preclinical trials, where the potential for the drug compound to improve human health is explored in both laboratory and animal studies. Preclinical trials represent a considerable change in terms of both context and probability of market launch. The end of preclinical trials is triggered by success in obtaining an Investigational New Drug (IND) license from the regulator and progression on to human clinical trials. Thus the research context moves from the laboratory and animal testing into the more externally regulated world of testing the efficacy of the drug via human clinical trials. The probability of successful market launch at the commencement of preclinical trials rises considerably from the 0.01% at the start of drug discovery and patenting to somewhere between 2 and 7% (PhRMA, 2007; Jagle, 1999). Preclinical trials not only mark the end of the exploration process, but also the end of conceptual and non-human trials; for this reason we expect that exploration returns will peak at this point.

After preclinical trials the firm makes a decision whether to try and move between the processes of exploration to exploitation. If the firm decides to enter the process of exploitation then it has to obtain an IND license to commence phase 1 human clinical trials. The decision to enter phase 1 trials is critical and the probability of market launch rises to 21.5% (DiMasi et al., 2003). Thus positive news that a firm will enter human clinical trials is indicative of considerable improvement in the likelihood of the drug making it to the market place. Clinical trials are subject to considerable external regulatory oversight. At this stage the key risk is that the drug will fail to attain the technical clinical end points in each of the three human clinical trials (phases 1, 2 and 3). The probability of success is not uniformly distributed across these three phases of human clinical trials. Empirical analysis by DiMasi (2002) observes that almost half of all decisions to abandon human clinical trials occur during phase 2, with 12.6% of all abandonment occurring at phase 3. The end of the exploitation process in this study is not, however, human clinical trials, but rather approval of an NDA clearing the way for legal marketing of the drug. Thus the fourth key stage of this R&D

process is the submission and outcome of an NDA to the regulatory authorities. Of course, there is a risk that the regulator will reject an application to grant marketing approval due to technical deficiencies in the application as a whole; however this risk is low and evidence from DiMasi (2001) indicates that the probability of success once a firm submits an NDA is about 90%.

Taking on board the ideas of March (1991) and Levinthal and March (1993) about the distinctive nature of exploration and exploitation processes we therefore hypothesize that the returns on each of the stages will differ. In particular we suggest that returns will peak at the end of exploration, namely preclinical trials, where the probability of market launch is about 2–7%. We also suggest that the returns to exploitation will peak at the end of this process, namely NDA, where the probability of market launch rises to 90%.

Hypothesis 2a. The returns to exploration investments will peak at the end of the process, namely preclinical trials.

Hypothesis 2b. The returns to exploitation investments will peak at the end of the process, namely NDA.

2.4. Firm size effects

DiMasi et al. (1995) are among many that suggest that small firms are less efficient at research than large firms. This may be occasioned by a combination of their lack of experience, their lack of resources, their inability to manage risk effectively and the lack of a proven track record for investors. For this reason one might expect the investor community to value small firm research intentions and outcomes less highly than that of larger firms. However, it has been argued that small firms are more flexible and less subject to hierarchical inefficiencies of larger enterprises, especially when engaged in smaller projects. Small biotechnology firms have played an important role in the development of bio-pharmaceuticals by acting as a bridge between exploration research by universities and exploitation by larger pharmaceutical firms with human clinical trial and marketing capabilities (Roijakkers and Hagedoorn, 2006). Early stage work in biotechnology is less capital intensive and relies on less complex, scale driven, organizational capabilities than the exploitation stage of the drug R&D process. Thus we posit that smaller firms will have a comparative advantage in exploration activities. We therefore explore with our data whether there is a small-firm effect in the market reaction to announcements.

The market may react to both announcements by small firms about the outcomes of their R&D activities and also about their intentions to enter into the next stage of the R&D process. When a small firm signals that it is committing to enter into the next micro stage of an R&D project, it is placing additional resource and capability strains upon the firm. Shareholders may be uncertain about the small firm's organizational capability to deliver upon its promises. Investor assessments of the value of intentions to enter into the next stage of the R&D process rely upon the competencies of management. How reliable are the assessments of the management of a small firm about their organizational capabilities to manage additional resource strains and make realistic assessments about the probabilities of their success? It may be that a shareholder in a small firm values information on the outcomes of R&D projects more than statements of intentions. This could be because outcomes communicate the ability of the firm to deliver upon its past R&D promises

In contrast, a larger firm is likely to be more experienced and have more resources and capabilities at its disposal. The market capitalization of a firm is a reflection of investors' expectations about the future financial earnings of the firm. Future earnings estimates rely on the firm's ability to convince investors of the value of its current competencies and its investment intentions. Their size, in terms of market capitalization, is a proxy for the strength of their resources and capabilities. It is also a proxy for the firm's ability to deliver on prior investment intentions. These firms have a track record of communication with shareholders on their investment intentions and the probability of converting intentions into positive outcomes. Shareholders of larger firms have the dual concern of getting product to the marketplace and replenishment of the R&D pipeline with new exploitation opportunities. Thus we expect that shareholders of large firms will be equally interested in news about the intentions of a large firm to enter the next stage of the R&D process and news of outcomes of such a stage.

Hypothesis 3a. Announcements by small firms that they are starting the next stage of the drug R&D process will be received less positively than the outcome of such a stage.

Hypothesis 3b. Announcement by large firms that they are starting the next stage of the drug R&D process will be as positively valued as an announcement of the outcome of such a stage.

2.5. Partnership effects

Frequently the R&D activities of biotechnology firms are undertaken with strategic alliance partners. There is a considerable body of evidence in the literature to indicate that the announcement of the formation of a strategic alliance can result in positive abnormal returns (Das et al., 1998; McConnell and Nantell, 1985; Merchant and Schendel, 2000; Xu, 2006). An interesting question here is whether shareholder investors anticipate all of the value creation effect of an R&D alliance at the alliance formation announcement. Alternatively, the activities of alliance partners may evolve over time in an unanticipated manner creating, or destroying, value in an R&D project. If the second scenario were the case then we would expect R&D activities conducted in alliance settings to generate different shareholder returns to in-house R&D projects at each of the six stages of progress.

The fact that alliances bring value is not in dispute. Danzon et al. (2005) argue that the presence of a large alliance partner in the conduct of human clinical trials raises the probability of success. They demonstrate that the success of phase 2 clinical trials rises by between 13 and 17% when the project is conducted in an alliance with a large partner compared to firms that undertake the phase 2 trial on their own. The success of phase 3 clinical trials rises by between 11 and 15% when a large partner is involved in the alliance. DiMasi (2002) reinforces this point, noting that an overall increase of 4.1% in the probability of success in human clinical trials would result in a US\$ 100 million saving in capitalized costs.

However, Alvarez and Barney (2001) argue that at the outset of many alliances small firms experience increases in share price even though over the life of the alliance large firms appropriate most of the value of the alliance: indeed 80% of small firms in their study felt that they were unfairly exploited by large partners, resulting in loss of value. The work of Robinson and Stuart (2007a) demonstrates that smaller firms who are less centrally embedded in a wider industry alliance network give up a greater amount of equity to alliance partners. Smaller less centrally embedded partners also receive smaller upfront payments (Robinson and Stuart, 2007b). Combined, this evidence leads us to believe that after alliance formation large partners continue to appropriate increasing amounts of the value created by the alliance.

Hypothesis 4. Announcements of R&D activities undertaken as part of an alliance partnership will be neutral or negative for small firms and positive for large firms.

3. Methods

Using the event study method, our dependent variable is the abnormal returns generated on the day of an announcement. Event studies assess the reaction of the financial markets to announcements of new information by a firm in terms of a rise or fall in share price over and above the normal expected behavior of that share. Underpinning the event study methodology is the semi-efficient market hypothesis, which argues that all publicly available information that offers insight into the present and future performance of a share is promptly digested by the market (Fama, 1991). Returns in excess of market performance should not persist beyond the short term required to assimilate the new information (typically a day).

Event studies have been employed in the literature to assess the impact both of regular required announcements (such as financial earnings statements), unexpected events, such as the senior executive death (Worrell et al., 1986) and disclosure of on-going projects, such as R&D (Narayanan et al., 2000), new product launches (Chaney et al., 1991), and FDA decisions on NDAs (Torabzadeh et al., 1998). Thus the method has a well established track record for assessing shareholder responses to incremental announcements of on-going corporate activities. Some prior event studies have, however, suffered from methodological defects that limited their validity. Thus we have been careful to apply the event study method as outlined by MacKinlay (1997), managing the problems of confounding events (McWilliams and Siegel, 1997), avoiding the use of a single expected-returns models (Chatterjee et al., 1998) and rising to the challenges of event studies in multi-country settings (Park, 2004).

3.1. Sample

We employed Biocentury, an online industry database that reports and classifies press releases by biopharmaceutical firms as our database and sampling frame. Our initial sample was the complete set of firms active in human therapeutics between 1996 and 2003 that were listed on the NASDAQ, London, Paris, Frankfurt and Milan stock exchanges. These 220 firms generated 2986 announcements about progress in the six stages of the R&D process (patenting, preclinical trials, phase 1, phase 2 and phase 3 human clinical trials, and NDA). Following good practice, all confounding events that occurred in a window of three days prior to the date of the R&D announcement through to three days after the announcement were identified and eliminated

(McWilliams and Siegel, 1997). Examples of confounding events included announcement of financial results, alliance formation, changes in management and other R&D events. This reduced the number of firms to 178 and announcements to 1277.

3.2. Measures

3.2.1. Independent variables—six stages of the R&D process

We explained earlier how we defined each of the six stages of the R&D process for drug development. Here we remind the reader that we labeled the granting of both patents and preclinical trials as exploration activities. We also labeled the three stages of human clinical trials (phases 1, 2, and 3) and NDA as exploitation activities. Our classification of patenting and preclinical trials as exploration and human trials (phases 1, 2 and 3) and NDA activities as exploitation are in line with prior biopharmaceutical studies (Rothaermel and Deeds, 2004: 209–210).

To ensure accuracy of coding of each event, the original source of the announcement was obtained through a combined search of Biocentury, the company website archived press releases and the Lexis-Nexus databases of news sources. The article or press release was read in full by a trained coder and the event was then classified into one of the six stages. Coding was cross-checked by the first author. Disagreements over coding were resolved through meetings of coders, where the source material was discussed. We also checked the dataset for the presence of repeat announcements, where the same information is re-announced in another publication or multiple times in the same publication. As repeat announcements do not provide new information to the market, they were excluded from the study.

3.2.2. Start of next stage of the R&D process

We were interested in whether the announcement of intention to start the next stage of the R&D process triggered abnormal returns. To test for Hypotheses 3a and 3b we coded each event as to whether or not it was an announcement regarding the initiation, or start, of one of the six micro stages of the R&D process (start = 1).

3.2.3. Firm size and age

We divided our firms into size classes. In our first stage of analysis we divided our data set into two and used the median capitalization of our whole sample as the cut-off point. We undertook tests to check if small

changes in classification altered the results, and we found that our results were robust.¹

In our second and finer-grained analysis of possible size effects, we use *R&D expenditure* as a proxy for firm size. This is a more exact measure that is only available for a sub-sample of firm observations. When exploring our size hypothesis using Ordinary Least Squares (OLS) models we split the sample around median R&D expenditure as a way of further controlling for size effects.

In line with many other previous studies we look to see if the age of a firm has an effect. We measure age as the number of years since firm foundation. This control is in keeping with other biotechnology studies (Rothaermel and Deeds, 2006; Sorensen and Stuart, 2000).

3.2.4. Alliances

Our data on alliances were gathered from Biocentury and checked with other sources. We were interested in whether firms that had alliances associated with their announcements would perform differently to those that did not. To test for Hypothesis 4 we coded each announcement as to whether or not the project was being undertaken with an alliance partner (alliance yes = 1).

3.2.5. Other control variables

We used cash balances as a control variable. The cash balance of a biotechnology firm is an important proxy for managerial discretion. Where cash balance is high management do not need to call upon capital markets for additional capital in the near term. A firm with relatively low cash balance will need to either curtail research expenditures or prepare for an additional call for funds to the capital market. In this case firms are likely to have lower managerial discretion.

Because the pull of cash can be offset by revenues, we used revenues as another control variable. Cash can be generated from milestone payments from alliance

¹ We also divided our sample into quartiles according to their market capitalization. Comparison of mean abnormal returns divided into size quartiles did not reveal that significant differences between quartiles, thus for the remainder of the paper we stratify the full sample around median market capitalization. It has been demonstrated in the Finance literature that average returns can vary according to the market value of a firm (Fama and French, 1992). This occurs for several reasons. The first is a measurement issue. Imagine that an event added US\$ 50 million to the value of a firm. For a firm valued at US\$ 100 million this would be a return of 50%, whereas for a firm valued at US\$ 1000 million it would be 5%. The second reason may be to do with signaling effects by the capital markets. Shareholders of large firms may be concerned with different issues from those of small firms. We take the view that the second effect is potentially important and explore this in our Hypothesis 3.

partners, contract work or in some cases product sales. Greater revenues may thus increase managerial discretion; therefore we control for a firm's revenues as recorded in the earnings report preceding the announcement.

We control for the timing of announcements over the industry lifecycle because it may influence returns. In 1996, the start of the period of study, the biopharmaceutical industry was still relatively young, whilst by 2003 the industry had matured considerably with hundreds of firms listed on stock exchanges. It is possible that, as more firms were listed on exchanges and thus more R&D announcements were released, the abnormal returns generated by such announcements changed as investor experience matured. Thus we have controlled for this effect by testing returns annually for differences across time, both for the sample as a whole and for each of the size classes of firm.

Finally, this study contains firms listed on both US and EU stock exchanges. To control for the possible impact of institutional differences we also controlled for this (EU = 1).

3.3. Dependent variable: abnormal returns

We calculated abnormal returns using the standard event study method as detailed by MacKinlay (1997). Following standard practice, expected or normal returns for company i are calculated as being a function of the returns obtained by the market where:

$$E_{it} = \alpha_i + \beta R_{mt} + \xi_{it}$$

R_{mt} is the continuously compounded realized returns on day t for a market index m . α is the regression constant derived from regressing R_{it} against R_{mt} . β_i is the regression coefficient derived from regressing R_{it} against R_{mt} . ξ_{it} is the error term derived from the regression with a mean of zero and a constant variance.

We applied a standard 160 estimation period starting at $t - 180$ days prior to the event day $t = 0$ and ending on day $t - 20$. Park (2004) warns that major terrorism events can temporarily distort market returns and this is problematic where estimation data cross these events. To manage this issue, we have excluded all NASDAQ listed company events during the period 11 September 2001 to the end of 2001.

Abnormal returns are then calculated as:

$$AR_{it} = R_i - E_{it}$$

R_{it} is the actual return on the day of announcement of an event. The selection of market index influences what the model will assign as the normal price behavior of

a given share. Most studies choose a single index and do not test the sensitivity of the abnormal return effect to selection of market index. Aware of criticisms of the event study method (Chatterjee et al., 1998), this study calculated expected returns using four models. Two market models regressed company returns against the local market composite index and a second model used local biotechnology industry index returns. Following their recommendation, we used both market models, as noted above, and the simpler average market index adjusted returns model as well as the average returns of the company itself. We report on the similarities between the different measures in our results section.

3.4. Calculating the day of announcement

In multi-country event studies, accurate identification of the day upon which an announcement first became available to the local stock market can be problematic (Park, 2004). In identifying day zero we have searched the company website press release archives and over 12,000 worldwide news sources contained in Lexis-Nexus to determine the time at which information contained in an announcement first became available to the market. We were also careful to consider the impact of local public holidays during which markets are closed. Similar care was used in determining day zero of confounding events. Thus we are confident that we have accurately identified day zero of our 1277 events and that confounding events have not occurred within a -3 to $+3$ day window of these events. To further reinforce our confidence in accurate identification of day zero all events were cross-checked by an independent researcher.

3.5. OLS model

It is common in the management stream of the event study literature to regress abnormal returns against a series of control variables in addition to the independent variables (in this case stage of R&D process using OLS multiple regression models). Examples of such an approach include Kale et al. (2002) and Narayanan et al. (2000). Price and market capitalization data were available for all events; however accounting and other control data were available only for a sub-set of the sample. For these firms we used abnormal returns on the day of the announcement as the dependent variable.

To reduce the potential for multicollinearity due to scale outliers, all continuous variables were converted into their log. The models reported in Table 5 do not exhibit multicollinearity issues. The VIFs in all cases were well below the suggested maximum of 10 (Myers,

1990; Bowerman and O'Connell, 1990). Furthermore the tolerances were all well above 0.2, which suggests the absence of a multicollinearity issue (Menard, 1995). The focus of this OLS analysis is to explore the significance of the coefficients of the independent variables (coded dummy variables with a value of 1 if present and 0 if not for all of the following: key stages of R&D process: patent, preclinical trials, phases 1, 2, 3 and NDA; start of stage; and alliances) and controls (log of R&D expenditure, cash, revenue, and firm age; stock exchange dummy EU = 1). We are not concerned with the R^2 of the models, which fall within the range of similar event studies in the management literature (Chen et al., 2002; Das et al., 1998; Kale et al., 2002; Narayanan et al., 2000).

4. Results

4.1. Checks for the robustness of the data and the overall response to announcements

We carefully explored the robustness of the data set and tested the extent to which the market responds to an announcement of incremental progress in the exploration–exploitation process on the day of that announcement as opposed to some other nearby date. Abnormal returns of +3.30% ($t = 16.263$, $p < .001$) are generated on the day of the announcement. In sharp contrast, returns on days -5 to $+5$ are not significantly different from zero, with the exception of day minus 2 where there is a small negative return of -0.25% ($p < .05$). It is clear that the event effect is primarily captured on day zero and therefore for the remainder of the paper we will report abnormal returns for day zero only.

We tested to see if returns differed significantly depending on which of the four expected returns models (two of which were based on market indices and two of which were constant mean return models) were used to calculate abnormal returns. We found that these returns were not significantly different from each other ($f = .0577$). In choosing which returns to report in this paper we decided, following convention, to use the local

index composite market model (in common with over 30 event studies published in the management field). We also note that the returns generated by this model were the lowest of the four models, with the highest returns of 3.80% being generated by the average adjusted local market index returns model.

We were also concerned with controlling for the effect of the industry life-cycle. The popular press suggests that, after 2001, the market reacted to announcements differently and more severely. A simple Fisher F test revealed that returns did not differ significantly across each of the years from 1996 to 2003 ($f = 1.377$). Thus we do not need to stratify the sample by year.

We also tested for size effects, coding firms as small, if their market capitalization was less than the median, and large if greater than the median in any given year. From Table 1 we can see that small firms generate significantly larger abnormal returns than large firms (4.01% versus 2.91%, $t = 2.94$). This difference in returns between small and large firms is significant at $p < .001$. (We also coded firms into quartiles in terms of market capitalization, but this did not reveal any further differences.) We will discuss small firm effects in more detail later.

4.2. Exploration–exploitation continuum

Tables 1 and 2 report the abnormal returns generated by exploration and exploitation announcements. Table 1 reports results grouped between the dyad of exploration–exploitation and Table 2 reports the results for each of the six types of announcement separately. According to both Tables 1 and 2, positive announcements on progress along the exploration–exploitation continuum generate positive returns for both large and small firms for each and every stage. There is strong evidence that positive news about all six stages of the R&D process is highly valued in the stock market, supporting Hypothesis 1.

To test for Hypothesis 2 we need to look at the trend of returns over all the six phases. We undertook a pair-wise analysis of differences between these six stages and these are reported in Table 2. When considering the results of

Table 1

Comparison of percentage abnormal returns (day zero): firm size and the exploration–exploitation dyad ($N = 1277$; large = 811; small = 466 firms; explore = 314; exploit = 958)

	All firms % abnormal return	Small firm events % abnormal return	Large firm events % abnormal return
All events	3.30*** (0.201)	4.01*** (0.376)	2.91*** (0.232)
Exploration events	3.98*** (0.436)	5.14*** (0.727)	3.00*** (0.510)
Exploitation events	3.08*** (0.226)	3.47*** (0.433)	2.88*** (0.260)
Differences	Explore > exploit*	Explore > exploit*	N.S. differences

Standard errors are reported in parenthesis. Significance of t -test * $p < .05$; ** $p < .01$; *** $p < .001$. N.S. = not significant.

Table 2
Percentage abnormal returns across the exploration exploitation six stage process ($n = 1\ 277$)

Stage of R&D process/size of firm	% mean abnormal return day 0 ^a	Standard error	Patent mean difference ^b	Preclinical mean diff. ^b	Phase 1 mean diff. ^b	Phase 2 mean diff. ^b	Phase 3 mean diff. ^b	NDA mean diff. ^b
All Patent ($n = 131$)	2.97 ^{****}	0.67						
Small firms ^c (62)	3.56 ^{****}	1.09						
Large firms (71)	2.47 ^{****}	0.82						
All Preclinical ($n = 190$)	4.70 ^{****}	0.56	-1.73	+2.40 ^{**}				
Small firms ^d (87)	6.21 ^{****}	0.95	-2.65	+3.16 [†]				
Large firms (103)	3.43 ^{****}	0.64	-0.96	+1.50				
All Phase 1 ($n = 264$)	2.30 ^{****}	0.36	-0.67	+2.33 ^{**}	-0.06			
Small firms (88)	3.04 ^{****}	0.74	+0.52	+2.59	-0.58			
Large firms (176)	1.93 ^{****}	0.39	+0.53	+1.78	+0.27			
All Phase 2 ($n = 319$)	2.37 ^{****}	0.35	+0.60	+2.33 ^{**}	-0.06	-1.25		
Small firms ^e (115)	3.62 ^{****}	0.70	-0.06	+2.59	-0.58	+0.54		
Large firms (204)	1.66 ^{****}	0.37	+0.81	+1.78	+0.27	-2.20 ^{**}		
All phase 3 ($n = 302$)	3.62 ^{****}	0.46	-0.65	+1.08	-1.32	-1.25	+2.56	
Small firms (92)	3.08 ^{****}	0.79	+0.48	+3.13	-0.04	+0.54	-4.15	
Large firms (210)	3.86 ^{****}	0.57	-1.39	-0.43	-2.20	-2.20 ^{**}	-1.85	
All NDA ($n = 84$)	6.18 ^{****}	0.86	-3.21 ^{**}	-1.48	-3.88 ^{**}	-3.81 ^{**}		
Small firms (26)	7.23 ^{****}	2.09	-3.67	-1.02	-4.19	-3.61		
Large firms (58)	5.71 ^{****}	0.83	-3.24 [†]	-2.28	-3.78 ^{****}	-4.05 ^{****}		

* $p < .05$. ** $p < .01$. *** $p < .001$. † $p < .10$.

^a Significance assessed using 2-tailed t -test.

^b Significance assessed using Games–Howell test, which does not assume balanced samples or equality of variance.

^c Small firms = less than sample median market capitalization in given year.

^d For preclinical trials, small firms generate greater returns than large. Comparison of means t -stat 2.344, significant at $p < .05$.

^e For phase 2 trials, small firms generate greater returns than large. Comparison of means t -stat 2.692, significant at $p < .01$.

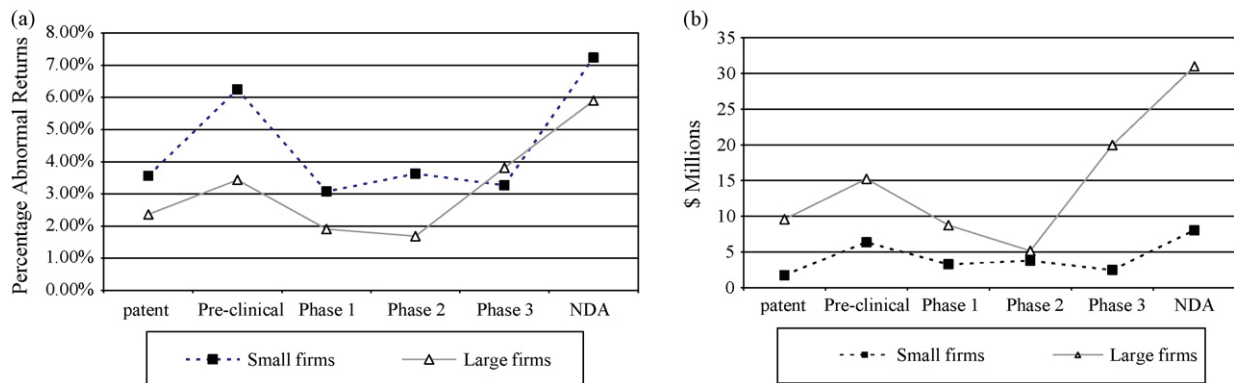


Fig. 1. (a) Trend analysis: exploration exploitation six stage cycle. Percentage abnormal returns. $N=1277$; large = 811; small = 466. (b) Trend analysis: exploration exploitation six stage cycle. US\$ millions abnormal returns. $N=1277$; large = 811; small = 466. Note: Polynomial contrasts, trend analysis confirms that for small firms the most significant trend is cubic trend ($F=8.081$, $p<.01$), whilst for large firms the most significant trend is quadratic ($F=9.368$, $p<.01$). In each case the peaks are at the end of exploration (preclinical trials) and exploitation (NDA).

the full sample, without consideration of size effects, the returns appear to peak at the end of both exploration (pre-clinical trials) and the end point of exploitation (NDA). This lends support for Hypotheses 2a and 2b.

4.3. Aggregate trend analysis

Stratification of the sample by company size into large and small firms using market capitalization median reinforces the view that returns vary over the R&D process, but introduces a much richer picture. First, as shown in Table 1, small firms achieve a higher return for exploration announcements than for exploitation announcements. (The reader should note that the very small sample of small firms achieving NDA means that the weight of this activity is small in our overall sample.) This result is the exact opposite of that posited by March (1991) and those that claim the exploration–exploitation dilemma is important. The same result cannot be said for large firms. Here it seems that there is no significant difference between exploration and exploitation activities. We discuss the significance of both these results later.

When we look at the shape of the returns over the individual stages of the R&D process, the split sample gives again a very rich picture. For small firms, preclinical trial announcements generate greater positive abnormal returns (6.21%) compared to those for phase 1 clinical trials (3.04%). These returns are statistically different from each other ($p<.10$). For large firms NDA announcements generate abnormal returns of 5.71%, which is greater than the returns associated with announcements by large firms of earlier stages of exploitation (phase 1 abnormal returns are 1.93% and phase 2 abnormal returns are 1.66%). For large firms the abnormal returns generated by NDA announcements

are statistically different from earlier stage exploitation events, namely phases 1 and 2 clinical trials ($p<.001$). However, the abnormal returns generated by large firms announcing preclinical trials are not significantly different from other announcements including NDA. Thus it appears there is some support for Hypothesis 2a for small firms and Hypothesis 2b for large firms.

Although pair-wise analysis is powerful, we probed the data further in two ways. First we undertook a trend analysis across the stages, and then we undertook a statistical analysis on a sub-sample of observations. There are clearly complex trends going on across the stages of product development. Fig. 1a illustrates the trend in percentage abnormal returns across the six stages of the exploration–exploitation cycle for the small and large firms reported separately. Traditionally the event study method only reports the percentage abnormal returns, as it is argued the key issue for a shareholder is percentage return, not the dollar change in firm value. It may be of interest for readers to visualize the dollar impact of these six micro stages of the R&D process. In Fig. 1b we convert percentage abnormal returns into US\$ millions (by multiplying the abnormal return on day 0 by the firm market valuation on the same day).² We can see the size effect in Fig. 1a and b. The percentage returns generated by small firms is greater than large firms in Fig. 1a, whilst in Fig. 1b that the raw dollar amount for small firms is lesser than for large firms.

The trends in Fig. 1a indicate that there are two peaks in terms of abnormal returns, namely preclinical trials and NDA, both of which are surrounded by troughs. We analyzed the trends of these six stages of the R&D

² We thank an anonymous reviewer for making this suggestion.

Table 3
Descriptive statistics and correlation matrix (sub-sample, $n=417$ events with full control data)

Variables	Mean	S.D.	Abnormal return (%)	Research and development (US\$ millions)	Cash (US\$ millions)	Revenue (US\$ millions)
Abnormal return (%)	3.28	0.65				
Research and development (US\$ millions)	10.18	10.96	-.080			
Cash (US\$ millions)	125.66	213.39	-.064	.761		
Revenue (US\$ millions)	6.84	18.48	-.017	.497	.402	
Firm age	11.23	4.91	.004	.125	.113	.237

$N=417$. Quarterly earnings report accounting data.

process to see if they were linear, U shaped quadratic or cubic (two turning points). In no case did we find a linear trend producing a good fit. Rather we found that the most significant trends were cubic for the sample as a whole ($f=9.949$, $p<.01$) and also for small firms ($f=5.430$, $p<.01$) and quadratic for large firms ($f=8.816$, $p<.01$). Each of these polynomials indicates that there are peaks at the end micro stages of exploration and exploitation. Fig. 1a visually demonstrates these trends, with all three trends showing the peaks to be the end of exploration (preclinical trials) and the end of exploitation (NDA). In conclusion, we can say that Hypothesis 2a predicts a local peak in exploration for preclinical trials. This Hypothesis 2a appears valid for large and small firms alike. A similar statement seems true for Hypothesis 2b about a local peak in exploitation for NDA; however, for small firms we have to be careful about the strength of this statement due to the small number of NDA observations.

4.4. Finer grained statistical analysis of a sub-sample of the data

We undertook multiple-regression on a sub-sample of 417 events for which full control data were available to obtain additional insights into Hypothesis 2. For this sub-sample, we control for firm size using R&D expenditures. Table 3 reports the descriptive statistics for the 417 announcements. Table 4 reports the descriptive statistics,

split by firm size. Although small firms have much lower R&D expenditure, cash balances and revenues than large firms; both small and large firms have a similar mean age of about 11 years.

Table 5 reports the results of our OLS regressions: models 1–4 are for small firms and models 5–8 are for large firms. Models 1 and 5 report the controls only. Models 2 and 6 add in the dummy variables for stage of R&D (to avoid collinear effects the dummy for phase 1 trials is dropped), enabling further inspection of Hypotheses 2a and 2b. Models 3 and 7 include a dummy variable for whether the announcement is regarding the initiation or start of one of the six micro stages of the R&D process (start = 1). This enables testing of Hypotheses 3a and 3b. Finally models 4 and 8 add the dummy for whether or not an R&D project announcement involves an alliance partner or not. This enables testing of Hypothesis 4.

Model 2 indicates that the returns for each stage of the R&D process for small firms are not significant. We believe this may be the consequence of small sample size: for our full sample the results are quite clear. For large firms, model 6 indicates that the end of exploration, namely preclinical trials, is positive ($p<.01$) and also that the coefficient for the end stage of exploration, namely NDA, is also positive ($p<.01$). From Table 5 we can see that this result continues to hold in models 6, 7 and 8, which all show positive coefficients for the preclinical ($p<.05$) and NDA stages of the R&D process ($p<.01$). Taking the evidence from Fig. 1a (trends of each stage)

Table 4
Descriptive statistics for small and large firm (sub-sample, $n=417$)

Variables	Small firms: 180 events		Large firms: 237 events	
	Mean	S.D.	Mean	S.D.
Abnormal return (%)	4.03	0.72	2.52	0.60
Research and development (US\$ millions)	3.11	1.85	15.55	11.93
Cash (US\$ millions)	33.72	42.25	195.50	259.94
Revenue (US\$ millions)	2.33	7.68	10.28	23.028
Firm age	11.56	6.06	11.00	3.830

Small = less than median R&D. Quarterly earnings report accounting data.

Table 5
Results of OLS analysis of abnormal returns (event day zero, sub-sample)

Variables	Small Firms: R&D < median $N = 180$				Large Firms: R&D > median $N = 237$			
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8
Intercept	0.137* (.067)	0.113 (.071)	0.112 (.070)	0.116 (.071)	0.042 (.59)	0.011 (.062)	0.013 (.062)	0.024 (.063)
Control variables								
R&D (US\$ millions)	-0.004 (.010)	-0.110 (.010)	-0.00007 (.10)	0.000 (.010)	-0.002 (.009)	0.000 (.010)	0.000 (.010)	-0.01 (.010)
Cash (US\$ millions)	-0.008 (.007)	-0.007 (.008)	-0.007 (.007)	-0.008 (.007)	0.003 (.004)	0.004 (.004)	0.004 (.004)	0.004 (.004)
Revenue (US\$ millions)	0.003 (.004)	0.001 (.004)	0.001 (.004)	0.001 (.004)	0.02 (.003)	0.001 (.003)	0.001 (.003)	0.000 (.003)
Firm age	-0.01 (.009)	-0.001 (.010)	0.00007 (.009)	0.00004 (.009)	0.000 (.011)	-0.003 (.011)	-0.003 (.003)	-0.003 (.011)
Stock exchange	0.000 (.012)	0.007 (.013)	.005 (.013)	0.006 (.023)	-0.029† (.016)	-0.022 (.016)	-0.022 (.011)	-0.023 (.016)
Independent variables								
Patent dummy		-0.012 (.022)	0.008 (.023)	-0.020 (.018)		0.024 (.019)	0.026 (.016)	0.026 (.019)
Preclinical dummy		-0.004 (.17)	-0.018 (.18)	-0.006 (.017)		0.029** (.013)	0.027* (.019)	0.029* (.013)
Phase 2 dummy		-0.007 (.017)	-0.008 (.017)	-0.013 (.018)		0.009 (.011)	0.009 (.013)	0.008 (.011)
Phase 3 dummy		-0.004 (.017)	-0.14 (.018)	-0.013 (.018)		0.019 (.012)	0.018 (.011)	.019 (.012)
NDA dummy		0.034 (.021)	0.020 (.022)	0.022 (.022)		0.057** (.018)	0.055** (.012)	0.053** (.019)
Start of stage = 1			-0.035* (.015)	-0.034* (.015)			-0.004 (.009)	-0.004 (.009)
Alliance = 1				-0.009 (.011)				0.008 (.008)
R^2	.018	.045	.073	.076	.021	.075	.076	.079
Change in f		0.943	5.014*	0.671		2.627*	0.154	0.844

Standard errors in parenthesis. All quarterly accounting data transformed into log to manage scale issues. * $p < .05$. ** $p < .01$. † $p < .10$.

and models 6, 7 and 8 from Table 5 we find further support for Hypotheses 2a and 2b for large firms which was discussed earlier.

4.5. *Announcements of intentions versus announcements of outcomes*

Many firms not only signal the results of an R&D stage, but also whether they start such a stage. For small firms the addition of the dummy for the start or initiation of any one of the six stages of the R&D process significantly improves the performance of model 3 over earlier models ($f=5.014$, $p<.05$). For small firms the start coefficient is significant and negative ($p<.05$). This indicates that announcements of the start of any of the six stages of the R&D process is of less value to shareholders than announcement of on-going progress or the results of any of the six stages. This supports Hypothesis 3a that states that for small firms announcements of intention are less valued than announcements of success. For large firms, the start coefficient is not significant for models 7 and 8. Thus Hypothesis 3b is supported. For large firms announcements of intention to start any of the six micro stages of the R&D process are as valued as announcements regarding the outcomes of each stage.

4.6. *Presence of alliances*

As noted above, we did explore whether the presence of alliances would alter the results. Looking at model 4, as hypothesized, the coefficient for alliances is negative for small firms; however this coefficient is not significant nor does this model significantly improve upon the performance of model 3 ($f=0.671$). As hypothesized for large firms the alliance coefficient is positive, however it is not statistically significant nor does model 8 represent a significant improvement over the performance of model 7 ($f=0.844$). Thus we find little support for Hypothesis 4 about the joint value of alliances and R&D success.

5. Discussion and implications

5.1. *Implications for firm-signaling of R&D to shareholders*

We believe that there are three important implications of our findings at the level of the firm. First, this study supports the view that investor-shareholders are not myopic in their analysis of firm value. They value all (positive) announcements of on-going exploration and exploitation activities but do not value all six micro

stages equally. Second, stock markets respond differently to announcements of on-going R&D activities from small and large firms, with implications for theorizing about exploration–exploitation and for the strategy of firms. Third, our results do shed light on potential additional value in alliances.

It has often been argued that because exploration returns are more distant there is a danger of underinvestment in risky R&D (March, 1991). These concerns have important consequences for policy debates and firm strategies. However, Teece (1986) among others has argued that such dangers can be overcome with strong institutional property regimes. Recognizing the issues at stake, institutions and markets have undergone some profound changes over the last fifteen years. In the bio-pharmaceutical markets search activities operate in a strong intellectual property regime. In addition, FDA and stock market regulation means that on-going exploration and exploitation activities are monitored by multiple actors and their value implications analyzed by the stock market.

Our data confirm that positive news of progress along all stages of the exploration–exploitation continuum is recognized and valued. We demonstrate that shareholders do not appear to be myopic in valuation of incremental R&D outputs or in the value of exploration. For the whole sample, the smallest returns reported were for patents at 2.47% ($p<.001$). The size and significance of this abnormal return is very considerable in the context of the event study literature in management. Narayanan et al. (2000) report considerably lower abnormal returns of 0.88% ($p<.01$) for innovation stage announcements, whilst Kale et al. (2002) report abnormal returns of 0.84% for alliance formation. Returns of 2.47% or greater are rare in the event study literature. Our results lend support to the work of Coriat and Orsi (2002) that biotechnology investor-shareholders are aware of the importance of exploration activities and respond very positively to positive announcements of on-going R&D activities being disclosed by management. Furthermore, results from Table 2 demonstrate that investors do not value announcements about each of the six micro stages of the R&D process equally. This suggests that stock markets are sophisticated in their valuations of R&D processes. They consider the relative value created by positive announcements from each of the six stages individually. The abnormal returns in response to each of the six stages are not the same.

Second, we consider the differential response of shareholders to positive R&D announcements by small and large firms over the R&D process. For large firms the local peaks of preclinical trials and NDA indicate that

shareholders are not drawn towards positive announcements about exploitation activities to the exclusion of exploration. It is fairly obvious why there is such a positive outcome for NDA as it reduces regulatory uncertainties about the legal sale of the drug and is highly valued. The significance of the preclinical trials for large firms indicates that shareholders are also interested in their exploration activities.

The lesson for small firms is different. Whilst shareholders do value positive announcements about all on-going R&D activities, there is some evidence that they value early stage exploration activity more highly than exploitation activities. We believe that this signals that small firms may have a “comparative advantage” in exploration research. This finding is in accord with the comments of Powell (1998) in his discussion of the evolution of the biotechnology industry. Some caution should be observed in taking this result too strongly. DiMasi et al. (1995) argue that both the duration and costs of preclinical exploration are greater for small than large pharmaceutical firms (but things may be changing as small firms become more sophisticated).

Related to the above point, our data suggest that small firms have to deliver results. We found from Table 5 that investor-shareholders of small firms appear to be skeptical about statements of intention to start any one of the six micro stages of the R&D process. This may be because these shareholders lack confidence in the ability of the small firm to deliver on their intentions. The message for small firms is perhaps to keep focused and craft communication strategies that build the confidence of shareholders in their demonstrated R&D competency through announcement of the outcomes of their R&D activities.

Our results have important implications for others that test the exploration–exploitation hypothesis. We find that small and large firms have different profiles of returns: in particular small firms seem to have higher exploration returns than large firms. This would help to explain why past studies may have yielded mixed results. Varying the mix of large and small firms in the sample could have caused differences in past findings.

It is also important to note that our findings may appear to run against the wisdom expounded by many industry executives who tend to suggest that small firms should try to move as fast as possible towards the exploitation phases as this is where the long-term future of the industry lies (Brooks, 2003; Edelson and Brown, 2004). These executives talk about firm survival driving this process. It is true to say from the data that late-stage exploitation events are valued by the market, but so also are earlier stages (Fig. 1a and b). The caveat to executive

advice on moving quickly to exploitation is that good quality exploration activity is worthwhile.

Third, let us consider the role of alliances in shareholder valuations of R&D success. The non-significance of alliances as a signal is interesting. There is strong evidence in the literature (reported earlier in this paper) that alliance formation has a strong positive impact upon shareholder wealth (Das et al., 1998). We know that alliance activity represents a considerable source of funds for R&D activities of biotechnology firms and that for small firms alliance activity is strongly associated with new product development (Rothaermel and Deeds, 2006; Zhang et al., 2007). In addition, R&D projects achieve higher rates of success at the later stages of human clinical trials if conducted in an alliance (Danzon et al., 2005), and thus implicitly lower R&D costs (DiMasi, 2002). So it may be that all the shareholder value of an alliance is recognized by abnormal returns generated at the alliance formation announcement rather than later when the R&D is completed.

In evaluating the alliance formation announcement, shareholders may have counterbalanced these value-enhancing benefits against the challenge of the ability of the large partner to capture increasing value over the life of the alliance. It may be that small firms are often at danger of long-term value appropriation by larger partners through unreasonable demands (Alvarez and Barney, 2001) or through the terms of the original contract, which may grant the larger partner more favorable equity stakes, board control, and reduced upfront payments (Robinson and Stuart, 2007a,b). Thus, the future positive and negative value creation and appropriation of R&D alliance activity between partners over the life of the alliance may have been fully captured at the announcement of the formation of the alliance. In these circumstances abnormal returns generated by R&D announcements after the alliance formation would not reflect the value of the alliance contract, but rather the underlying R&D activities themselves. Our evidence in Table 5 appears to support this view. The alliance dummy variable is therefore not significant in any of our models.

We do acknowledge several potential limitations of our study. First, we only study positive announcements of R&D activity by our sample firms. As indicated earlier the drug R&D process is risky. Few drug compounds successfully progress through the process of R&D and onto the market place. Our sample firms do report negative findings to the stock market and it may react differently to these announcements. A practical difficulty that we faced in including negative announcements in our study

was the lower frequency with which negative announcements were unambiguously published by the sample firms. Many negative announcements coincided with other confounding events, such as announcements of positive news about other R&D projects. The net effect of a lower frequency of public announcement of negative events and a high incidence of confounding events made the conduct of an event study using negative events impractical. It should be noted that the problems we encountered are not confined to the bio-pharmaceutical sector (Kelm et al., 1995). We recommend that, as the database of announcements by these firms grows over time, future studies might seek to undertake an event study that employs both positive and negative announcements of R&D activities.

Second, it might be argued that our exploration findings are subject to endogeneity in the context of the broader industry equilibrium of which they are a part. It could be argued that the small firms in our study are a self-selected sample of firms with past success in blue skies biotechnology R&D that are formed with the purpose of exploitation of their findings. Descriptive statistics from table four indicate that our small firms are a little older than our large firms (11.56 years old versus 11 years old). We believe that our sample firms are representative of the wider community of entrepreneurial bio-pharmaceutical firms and thus, whilst recognizing the possibility of some endogeneity in our study, are not overly concerned that this has distorted our findings.

5.2. *Implications for public policy*

What does all this mean for public policy? We believe that there are three important implications of our work for research intensive firms. First, the data support the belief that stock markets monitor and respond to positive announcements about exploration activities, even of relatively small entrepreneurial firms. The stock market appears to be able to monitor and respond differentially to the nuances of the R&D process, as evidenced by the differential returns that it awards to the six stages of the R&D process that we focused upon in the bio-pharmaceuticals industry. A central feature of these six milestone stages is that each is subject to a measure of independent external review by actors with industry-specific knowledge and often access to private firm knowledge. For example a patent is subject to the assessment of independent patent assessors; a new drug marketing approval arises from a process of review of private firm clinical data by a knowledgeable external and independent agent in the form of national regulatory bodies such as the FDA. As economies become

more knowledge- and research-intensive it is encouraging that stock markets have the ability to not only provide capital to early stage, loss-making firms, but also that, in the presence of milestones that are subject to external validation, they are able to assess the long-term impact of positive announcements of incremental developments of a firm's pool of knowledge into its market valuation.

Second, the market is able to assess the differential value created by various stages of the exploration–exploitation R&D process in large part due to the existence of clear milestones within the exploration process itself. These milestones facilitate the external assessment of the value of the exploration activities of firms, demonstrating the need for highly specialized, firm-specific private knowledge of the internal activities of the firm. Where valuation is determined by internal, firm-specific, private knowledge, stock markets will be less well placed to value exploration investments (Tylecote and Ramirez, 2006).

Third, the previous two conclusions lead us to our central research policy implication. Where innovation is of strategic importance to national and regional economies and where such innovation involves lengthy creation processes and substantial capital requirements there is a need for national bodies and stock markets to consider the development of structural mechanisms to assist valuation of exploration activities through methods other than earnings statements. The intellectual property rights regime and regulatory environment that exists in the bio-pharmaceutical industry may not have as its primary purpose the creation of investment milestones for investors, however their existence is a powerful incentive to investment in this strategically important sector. Stock markets play an important role in the provision of capital and incentives to encourage scientist entrepreneurs to convert their ideas into products with mass market benefits through the process of commercial exploitation. Policy makers should consider what other sectors in the economy that have the features of lengthy development time horizons, capital intensity and strategic importance to society they wish to encourage investors to make financial commitments to. In supporting the sustainability of these financial commitments over the lifecycle of R&D, policy makers should consider what mechanisms they can put in place that support innovation through appropriation regimes that encourage innovation and put in place milestones that reveal the incremental value created by such innovation over the R&D lifecycle without requiring revelation of private information to public shareholders that might destroy intellectual property rights, be they patents or commercial secrets.

Acknowledgements

Thanks to the two anonymous reviewers and the editor Woody Powell who with great patience helped improve earlier drafts of this paper. We also recognize the participants of EGOS 2005, sub-theme 2 Unlocking Biotech, especially Mark Ebers, Woody Powell, and Vincent Mangematin for comments and suggestions that have helped shape this paper. Thanks to Don Bergh, David Deeds, Patrick Gibbons, Robert Grant, Erik Larsen, John McCallig, Colm O’Gorman, Dorota Piaskowska, Simon Peck, Amir Sasson and Jing Zhang for comments and suggestions on earlier drafts. We thank the participants of the University of St. Andrews, School of Management seminar series for their valuable comments and suggestions. We also thank Jude Bolger, Liz Corcoran, Linda Maguire, Laurence O’Shaunessy, Aoife Power, Anne Marie Raftice and Christina Vassou for their assistance in data collection. We acknowledge research funding from the UCD Business School, Business Research Fund and the UK EBK-ESRC Programme.

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