Valuation Implications of Pharmaceutical Companies' R&D Regulatory Approval Notifications

By

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ABSTRACT

This paper examines shareholder wealth effects surrounding applications to, and approvals by, the United States Food and Drug Administration (FDA) for firms listed on the New York (NYSE) and London (LSE) stock exchanges. Applications to the FDA for drug approvals significantly increase shareholder wealth for NYSE firms only. The increase is driven by applications for enhancements to existing drugs, with the market anticipating the application, thus suggesting information leakage. FDA approvals also significantly increase shareholder wealth in both markets. However, there is no evidence of information leakage and the significant post-event abnormal returns support the attention-grabbing hypothesis. Enhanced drug approvals are value-relevant for both markets, which highlights the contribution of real-options to firm value.

Keywords: **Event study; Food and Drug Administration (FDA); London Stock Exchange (LSE);New York Stock Exchange (NYSE); pharmaceutical firms; real-options; Research & Development (R&D)**

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Introduction

This paper investigates shareholder wealth effects for pharmaceutical firms listed on the New York (NYSE) and London (LSE) stock exchanges that applied to the US Food and Drug Administration (FDA) for regulatory approval. In the pharmaceuticals sector, drug-in-progress announcements are a significant performance indicator and have been shown to significantly increase shareholder wealth along the various stages of the exploration-exploitation continuum (McNamara & Baden-Fuller, 2007; Dedman, Lin, Prakash & Chang, 2008). In such an environment, the need to attract and maintain investor confidence is a non-negotiable requirement, of which the pharmaceuticals sector is acutely aware. Consequently, studies investigating shareholder wealth effects surrounding drug development announcements have an important role in informing a range of stakeholders. In intangibles-intensive industries, non-financial performance indicators provide important signals to investors of firm performance, and can substitute for financial disclosure (Amir & Lev, 1996; Eccles, Herz, Keegan & Phillips, 2001; Ely, Simko & Thomas, 2003; Espinosa, Gietzmann & Raonic, 2009). The aim of this paper is to contribute to the literature by investigating wealth effects surrounding the exploitation stage of the drug development process. For the first time, we evaluate the contribution to shareholder wealth of firms developing either new drugs or enhancements to existing drugs.

The potential for key decision-makers within the firm to exploit the private information they possess regarding the likelihood of a successful drug development exists. This is particularly true in the final days before the public announcement, when the discussion on the merits of the application between the FDA and the firm has nearly been

concluded. Thus, this paper makes a further contribution by shedding light on whether information leakages exist in the period surrounding the regulatory announcement.

We develop five hypotheses with the aim of providing a new insight into the exploitation stage of R&D which includes applications to the FDA for drug approval, and announcements by the FDA that a drug has been approved for marketing and eventually, for sale. Furthermore, we examine information leakage, if any, surrounding regulatory drug applications made to and approvals by the FDA. We further test as to whether the capital markets value enhancements to existing drugs, and focus our attention on the post-announcement period to quantify the market reaction as a test of the attention-grabbing hypothesis. Standard event study methodology is utilised to test the five hypotheses that we have developed in the study over a 43-day event window.

This study contributes to the literature in several ways. First, we divide the exploitation stage into applications and approvals in order to provide a finely grained analysis of shareholder wealth effects at this pivotal stage of the R&D process, which highlights significant differences between the NYSE and LSE listed firms. As expected, approvals significantly increase shareholder wealth in both markets, but applications are only value-relevant for NYSE firms. For the UK, a significant market reaction around approvals is consistent with Dedman et al. (2008), who conclude that UK investors demand further progress through the drug development process before they capitalise R&D expenditures. The fact that the LSE listed stocks' applications are not value-relevant provides important insights for UK investors, by confirming that approvals are the key driver of shareholder value at the exploitation stage of R&D. Our sample period is from 1991 to 2008, whereas Dedman et al.'s period starts in 1990 and ends in 1998. The longer sample period allows for a

sufficient sample size to disentangle shareholder wealth effects, not only for approvals but also for applications. An understanding of precisely when returns accrue from R&D at the exploitation stage is of significant importance to investors. The more extensive sample permits us to evaluate, for the first time, the contribution to the shareholder wealth of firms seeking regulatory approval for enhancements to existing drugs.

Second, we distinguish between new and enhanced drug applications to the FDA. In economic terms, significant increases in shareholder wealth surrounding applications and approvals of enhanced drugs should highlight the importance of real (follow-on) options in creating wealth in the pharmaceutical industry. Third , it is common practice in the literature to report the mean abnormal return on the event day, and cumulative abnormal returns (CARs) for various holding periods, typically centred on the event day (e.g. two days' CAR from day 0 to +1) [McNamara & Baden-Fuller, 2007; Dedman, Lin, Prakash & Chang, 2008]. Given the reported significance of the mean and CARs, it is evident that a post-event market reaction occurs. We focus our analysis on the post-event period and report significant mean and CARs for both markets and explain this result in the context of the attention-grabbing hypothesis, which, in contrast to what would otherwise be inconsistent with the efficient markets hypothesis, provides a behavioural explanation for observed price effects the day after an attention-grabbing event. Since this model highlights the behaviour of individual investors, an important extension of this paper would be to directly investigate the composition of pharmaceutical firms' investor base and explore their contribution to shareholder wealth effects at various stages of the R&D process.

This paper is organised as follows: Section 2 outlines the key features of the pharmaceuticals industry and provides an economic rationale for disclosure in general and

specifically for managers voluntarily disclosing information in relation to the drug development process. It also briefly summarises the stages of the FDA drug approval process. Section 3 reviews the literature and motivation for this study. Section 4 develops our hypotheses, while Section 5 discusses our methodological approach and sample. Our findings are discussed in Section 6, with Section 7 concluding our study.

2. Economic rationale and industry background

In general, idiosyncratic features of the pharmaceutical industry present challenges, even for the most sophisticated of investors, when trying to derive an estimate of fundamental value. Conventional equity valuation models are difficult to apply, owing to the complexity of the science underpinning products and technologies developed, long development lead times, significant ongoing capital requirements, complex intellectual property issues and regulatory hurdles. These issues are particularly acute for the many small and medium sized enterprises (SMEs) in this industry which represent the vast majority of firms in the UK (Dedman et al., 2008).[1] In contrast to large firms, SMEs in this industry often do not have products to sell to generate earnings. Consequently, an important empirical performance attribute commonly observed is sustained negative-earnings, which is the result of significant investment in R&D, and to comply with SSAP 13, most of this expenditure is expensed immediately. While reported earnings are normally an important determinant of value, key performance indicators (KPIs) for loss-making pharmaceuticals include retained cash, rate of cash expenditure, or 'burn-rate', and the timing and source of additional capital requirements.[2] It is intuitively obvious that from a firm's perspective, attracting investors in such a complex business environment is a challenge. This sentiment is echoed by the Chief

Executive of the UK's Bioindustry Association when she states, in the foreword to their code of best practice:

> "*Attracting investment has always been crucial for the bioscience industry. Investor confidence remains a fundamental and non-negotiable requirement of a successful sector…..…Our companies face unique challenges when seeking to develop, trial and bring new products to market*…[consequently] *Establishing investor confidence on a long term and sustained basis is a challenge for us all*". Bioindustry Association's 'Best Practice Guidance on Financial and Corporate Communications' (2004).[3]

From an economic perspective, well-functioning capital markets require resolution of the information, or "lemons", problem (Akerlof, 1970). Corporate disclosure solves this problem in capital markets and has been categorised into mandatory regulated financial statements and voluntarily disclosed information, with external information intermediaries such as financial analysts also reducing the information gap (Healy & Palepu, 2001). The complexity of the pharmaceutical industry accentuates information asymmetry between investors and entrepreneurs. A key value driver for biotech-pharma firms is the non-financial announcements from outcomes at various stages of the drug approval process. An announcement of a firm's success, at any stage of the drug development process, is at the discretion of management and, as such, falls into the voluntary disclosure category and is classified in the literature as a non-financial performance indicator. More specifically, the decision to disclose voluntary information related to the drug development process is modelled within a game-theoretic context (Dedman et al., 2008). The argument is that voluntary disclosure is a special case of game theory, where an entity will disclose positive information while suppressing negative information, an outcome of the entity's optimising behaviour (Dye, 2001). Once disclosed, the real-options approach provides a theoretical rationale explaining why key non-financial performance variables are significant value

drivers of biotech-pharma companies, and that financial performance indicators are informative when released contemporaneously with non-financial performance indicators, such as drugs-in-progress (Eccles et al., 2001; Ely et al., 2003; Espinosa et al., 2009).

The US Food and Drug Administration (FDA) regulatory approval process is classified into 'micro-stages' (McNamara & Baden-Fuller, 2007). Once a new chemical entity (NCE) is discovered, Stage 1 is the award of a patent. Pre-clinical trials are the second stage, and involve laboratory and animal studies. If preclinical trials are successful, the developing firm progresses to the third stage, which incorporates three phases of human clinical trials: phase I assesses the safety of the drug on humans; phase II evaluates effectiveness at various doses for a larger group of subjects; and Phase III involves administering the drug to a large number of patients who meet the selection criteria. Successful Stage 3 trials open up the possibility of progressing to Stage 4, which is the submission of a new drug application (NDA) to regulators. Approval of an application grants marketing rights for the drug to be sold legally, which is the 5^{th} stage of the process.

It is argued in the literature that each stage represents definable progress for the R&D process, with patenting and pre-clinical trials categorised as basic exploration research, and with human clinical trials and NDA classified as exploitation (DiMasi, 1995; DiMasi, Hansen & Grabowski, 2003; Rothaernel & Deeds, 2004; McNamara and Baden-Fuller, 2007).[4] Viewed through the lens of the likelihood of success, each development stage represents progress and provides a key insight into drug development. The development stage involves the identification and development of new chemical entities. These entities

are new discoveries by the company in the early part of the drug discovery stage, which after undergoing clinical trials, could translate into a drug that could be a cure for some disease.

One estimate is that five out of 5,000 new chemical entities proceed to human clinical trials, with only one likely to be granted approval, with an average total time of 12 years from discovery to market (Dedman et al., 2008).[5] It is generally accepted that mandatory regulated financial statements are less important in providing an insight into the likelihood of the marketing success of a developmental drug. This is reflected in the relatively lower earnings quality for intangibles-intensive industries, such as the pharmaceutical industry (Espinosa et al., 2009). Game theory predicts that strategically optimising managers will disclose positive news while suppressing negative news about their drug development. Consequently, a reasonable conjecture is that if managers voluntarily disclose non-financial information to the market, they, at least, expect it to be value-relevant. Whether the market values information that is disclosed voluntarily by the firm is an empirical issue and this study sheds some light on it.

3. Literature review

Empirical evidence reports that firms engaging in enhanced disclosure benefit from obtaining relatively lower cost of equity and debt capital and reduced bid-ask spreads with enhanced disclosure being shown to be informative in relation to predicting future earnings (Botosan, 1997; Botosan & Pulmee, 2001; Sengupta, 1998; Welker, 1995; Healy et al., 1999; Gelb and Zarowin, 2002).[6] A range of non-financial disclosure metrics for a number of intangibles-intensive industries is shown to be value-relevant in the US. Amir and Lev (1996)

highlight the value relevance of non-financial disclosure in the wireless communications industry. In isolation, financial information is reported to be largely value-irrelevant, but when combined with a proxy for growth becomes informative. For the US biotech-pharma sector, Ely et al. (2003) arrive at a similar conclusion to Amir & Lev (1996): aggregate earnings become informative when combined with a variable they construct to capture a portfolio of drugs' likelihood of success.

In the US, 1962 is a significant turning point in the history of the FDA drug approval process. The Kefauver-Harris Amendments of 1962 to The Pure Food and Drug Act of 1906 require proof of the safety and efficacy of drugs prior to marketing (Dranove & Olsen, 1994; Sakar & de Jong, 2006). Regulatory impositions increase the cost and time it takes to bring new drugs to market, and spawn a literature focusing on shareholder wealth effects around FDA announcements. Early studies evaluate FDA approvals, rejections, recalls, disciplinary decisions, spill-over effects and the extent of information leakage (Bosch & Lee, 1994; Hingorani et al., 1994; Dranone & Olsen, 1994; Torabzadeh et al., 1998; Sharma & Lacey, 2004). Collectively, this literature reports significant increases in shareholder wealth for drug approvals, decreases for rejections and recalls, spill-over effects on competitors, and evidence of information leakage. More recent investigations seek to unpick the finer aspects of the information content of the FDA drug approval process. For a sample of 178 bio-pharmaceutical firms with 1,277 announcements from 1996 to 2003 listed on NASDAQ, London, Paris, Frankfurt and Milan stock exchanges, McNamara & Baden-Fuller (2007) assess the market's reaction to announcements along the six micro-stages of drug development. For each of the six micro-stages, they report a significant positive market reaction, with evidence of

'peaks' in the market's reaction at the latter end of exploration and exploitation stages. They also report that investors value exploration and exploitation announcements by large firms and focused exploration activities for small firms. However, projects which are part of a strategic alliance partnership, a common practice in the industry, are not value-relevant.

Dedman et al. (2008) analyse the UK biotechnology/pharmaceutical sector from 1990-1998. They evaluate shareholder wealth effects along the exploration-exploitation drug development continuum and explore whether firms' announcements are concentrated at the exploration stage for smaller firms and the exploitation stage for larger, dominant firms. Their findings confirm the relative importance of drug approval announcements, with approvals significantly increasing shareholder wealth. Consistent with the low earnings quality typically purported to be a feature of an intangibles-intensive high R&D industry, earnings are not found to be value-relevant. They also report that managers, consistent with Dye's (2001) theory of voluntary disclosure, actively suppress news related to unfavourable outcomes from drug development. Dedman et al. (2008) conclude that it appears that UK investors demanded '*...further progress through the drug development before they capitalized R&D expenditures*'.

Our paper is motivated by a number of factors. To date, there has been limited market-based analysis of the strategically important UK pharmaceutical industry. It is important, therefore, that we further understand the market's assessment of drug-in-progress announcements. As noted earlier, the bio-pharma industry regards attracting investment and maintaining market confidence as a non-negotiable requirement in ensuring a successful sector. Consequently, an updated analysis of shareholder wealth effects has the potential to offer important insights for a range of stakeholders. Over the last twenty years, globalisation has led

to industry effects dominating country effects in developed markets in firm level returns (Flavin, 2004; Wang et al., 2003; Phylaktis & Xia, 2006). The rising dominance of industry effects leads to the reorganisation of practitioners from country to industry analysts. By investigating shareholder wealth effects for firms listed on the NYSE and LSE that apply to the same regulator at the same stage of R&D, we hold both parameters constant. This allows investors to compare absolute returns across markets. Such a cross country comparison has the potential to provide insights for pharmaceuticals sector financial analysts, and investors, *inter alia*.

4. Hypothesis development

In the context of our prior discussions, we develop a number of testable hypotheses. Dedman et al. (2008) conclude that managers suppress negative news about drug development. The empirically observable low probability of successfully bringing a new drug to market mirrors the fact that the vast majority of projects are unsuccessful. If all outcomes were disclosed at each stage of the drug development process, we would expect a much higher incidence of unsuccessful drug development announcements. Empirically, we observe a disproportionate disclosure of success relative to failures. It can be argued, therefore, that managers' disclosure behaviour is consistent with self-interest, as predicted by game theory. A new drug application (NDA) is made at the discretion of managers and such an application reflects a successful outcome from a large-scale trial designed to assess safety and effectiveness (Stage 3, phase III).[7] The decision to submit a license application clearly

reflects managers' belief that the project is a worthwhile investment.[8] We have our first testable hypothesis, stated in alternative form as:

> **H_1***: An announcement by a firm of a new drug application will, on average, increase shareholder wealth.*

Given the importance of the drug development process as a key performance indicator in the pharmaceuticals industry, and the documented significant positive abnormal returns attributed to the announcement of positive outcomes, the incentive exists for information leakage. The US empirical evidence is ambiguous (Bosch & Lee, 1994; Torabzadeh et al., 2001). The filing of an application initiates a rigorous examination process of test results and likely clarifications by the firm to the FDA, which culminates in the final decision to approve or otherwise. In the period between NDA and the announcement of the outcome of the application, regular communication ensues between the firm and the FDA. It can be argued, therefore, that this post-application discourse will allow key decision-makers within the company to assess, with increasing confidence, the likely outcome of the NDA. Therefore, there is potential inside knowledge of the probable outcome in the days prior to the announcement. If NDAs and approvals are value-relevant, and information leakage occurs and is significant, then we would expect to observe significant abnormal returns over the pre-event period, which we would expect to be positive. Consequently, we hypothesise that:

> **H2:** *Significant positive abnormal returns in the pre-event period are evidence of information leakage.*

FDA approval of a new drug application resolves uncertainty for investors. A consistent finding reported in the empirical literature is a significant positive market reaction to drug approval announcements across a number of markets (Bosch & Lee, 1994; McNamara & Baden-Fuller, 2007; Dedman et al., 2008). We hypothesise that:

H_3: *FDA Approval of a NDA will, on average, increase shareholder wealth.*

The empirical evidence clearly highlights that the announcement of successful outcomes at various stages of the drug development process are news events, with drug approvals being major news events associated with significant contemporaneous abnormal return 'peaks' (McNamara & Baden-Fuller, 2007). Barber & Odean (2008) provide a model and empirical evidence explaining how individual investors gravitate to 'attention-grabbing' stocks. Odean (1999) and Barber & Odean (2008) argue that individual investors are more likely to buy, rather than sell, stocks which catch their attention. A key prediction from Barber & Odean's (2008) model is that individual investors actively buy stocks on high-attention days, and that, to a large extent, individual investors focus on past returns for stocks they sell, while for buys their focus is on future returns. In the context of our analysis, this finding opens up the possibility of post-event abnormal returns.[9] As FDA approvals are 'good news' items, we would expect post-event abnormal returns to be positive. For our fourth hypothesis, we conjecture that:

H_4: *Positive post-event abnormal returns for FDA approval announcements support the attention-grabbing hypothesis.*

Next, we investigate whether the market differentiates between applications which enhance existing drugs versus applications for new molecular entities. The FDA defines a new molecular entity as an active ingredient that has never before been marketed in the United States in any form. In simple terms, a new molecular entity is a newly discovered drug for disease treatment. Enhancements cover previously approved drugs with a new indication, formulation combination, manufacturing process, over-the-counter switch, dosage regimen, labelling revision, formulation revision, supplement or generic drug.[10]

A marketing approval for an enhanced treatment for an existing drug enables managers to exploit their investment opportunity choices or real-options as they arise. Examples of real-options that managers face are the option to: postpone, abandon or rescale an investment; change the technical nature of an investment; invest in research and development (R&D); and create options to produce new products and options to make subsequent or follow-on investments (growth options) which would not have otherwise been possible.

The inability of traditional investment appraisal techniques to capture the value inherent in real-options leads to an underestimation of a project's net present value (NPV). However, it is generally accepted that the application of real-options as an investment appraisal technique has been limited due to its complexity and because the evidence examining the association between decision-makers' intuition and real-option theory is mixed (Busby & Pitts, 1997; Howell & Jägle, 1997; Remer, Ang & Baden-Fuller, 2001; Verbeeten, 2006). While it is evident that there is considerable variation in the application and understanding of real-options generally, the biotechnology/pharmaceuticals sector is

often cited as an industry where real options analysis is applicable and where firms' market value can be considered as the value of a basket of real options on their R&D portfolio (Ely et al., 2003; Woerner & Grupp, 2003; Hartman & Hassan, 2006). Real-options is also the application of option-pricing to non-financial instruments. It provides concrete valuation procedures (real-options pricing) and a conceptual framework (real-options reasoning) for evaluating and understanding investment decisions by firms (Merton, 1998; Pfeiffer & Schneider, 2010). In contrast to standard discounted cash-flow investment appraisal techniques, such as NPV, it is argued that real-options capture the flexibility of managers to react to new information as it arrives throughout the life of a project.

A reasonable assumption underpinning real-options is that it will be exercised if it is in the interests of the firm to do so. This is consistent with the basic principle underpinning financial options – if an option is in-the-money, it will be exercised. A logical extension of this argument is that management believes that their decision to execute a follow-on option (that is, to apply for regulatory approval for enhancements to existing drugs) reflects their belief that the real-option has intrinsic value which, if exercised, has the potential to enhance firm value. The extent to which follow-on options contribute to enterprise value, assessed in terms of shareholder wealth, provides an objective empirical analysis of benefits to investors from managements' ability to extract additional value from firms' R&D portfolios. This leads to our fifth, and final, testable hypothesis:

H_5: *Enhancements to existing drugs create follow-on options which increase firm value.*

A market response analysis of follow-on options has the potential to make a significant contribution to the literature. There is general agreement that the flexibility and uncertainty inherent in R&D in the pharmaceuticals sector lends itself to a real-options framework, but there is considerable variation in terms of decision-makers' conceptual understanding of this approach and the ability of firms to implement it systematically as an investment appraisal technique. Our *ex-post* analysis allows for clear identification of follow-on options which have been exercised, and provides an estimate of their market value. This is regardless of whether the decision-maker exercising the option employed option-pricing methodology, *ex-ante*, to evaluate the investment opportunity, or understood conceptually that they were executing a follow-on option in the absence of a pricing methodology.

5. Research Design

In terms of evaluating tangible performance benefits from exploration-exploitation activities in the pharmaceuticals industry, a number of studies adopt an accounting approach, concluding that exploitation research is significantly more financially rewarding (Bayus et al., 2003; Rothaernel, 2001a, 2001b). As previously discussed, given lower earnings quality and the tendency for firms to report persistent negative earnings, we employ event study methodology to avoid these problems and to assess the information content and associated shareholder wealth affects, if any, from announcements. This approach allows us to isolate the market's assessment of the value created from incremental R&D investment before revenues are generated.

5.1. Sample

The sample of firms in this study is made up of FDA regulatory application and approval notices issued to UK listed pharmaceutical companies from January 1992 to December 2007 for approvals and from January 1991 to December 2007 for applications. For US sampled firms, the data cover the period from January 1998 to 2008 for applications and from 2002 to 2008 for approvals. Regulatory approval and application notices are collected from Perfect Information System, FDA, and Pharmaceutical Research and Manufacturers of America websites covering the study period. All US firms are New York Stock Exchange listed. Share price data for the pharmaceutical companies are collected from Datastream. Each observation included in the sample must have data available for the computation of market model parameters and there must be no contaminated news announcement in the 21 days around the announcement date. Sample firms total 215 (91) for NYSE (LSE) for NDA applications and 209 (124) for approvals, respectively, over the sample period.

5.*2.* *Methodology*

We employ event study methodology, with the market model used to generate expected returns, to quantify the impact on shareholder wealth of a firm's application to the FDA for an approval, and the FDA's approval of a new or enhanced drug, allowing firms to market and sell the drug.[11] Abnormal returns are computed for a 43-day test period (from day -21 to +21) using the market model estimated from day -150 to -22:

$$R_{i,t} = \alpha + \beta(R_{m,t}) + \varepsilon_{i,t} \qquad (1)$$

where ε_{it} is the abnormal returns accruing to shareholders in firm *i* on day *t* relative to the day of the announcement, R_{it} is the log daily returns to stockholders adjusted for dividends and other capital changes, R_{mt} is the daily natural log returns on the Financial Times All Stock Index, employed for the LSE listed stocks, and Datastream Total US market index is used as the benchmark index for NYSE listed stocks, with α and β as parameter estimates. Scholes and Williams' (1977) procedure is adopted to adjust the beta estimated in equation 1 to account for the possibility of asynchronous prices when calculating returns. Mean abnormal returns as a measure of central tendency are susceptible to the influence of outliers. To ameliorate their influences and corroborate the results for the parametric event study, Corrado's (1989) non-parametric rank test is also employed as a robustness check. Likewise, when computing the test statistic for cumulative abnormal returns, the robust standard error reported in Hamill et al. (2002) is adopted.[12]

6. Results

INSERT TABLE 1 ABOUT HERE

6.0. *New Drug Applications*

The average number of days it takes to be granted marketing approval for NDAs is slightly shorter for US listed firms than for non-USA listed firms by about 10 days. On average, it takes about 540 days between the filing of an application and a new drug approval to be granted for US listed firms. For all others, the average is about 550 days.[13]

It must be noted that it is not a foregone conclusion that an approval will be forthcoming following an application. The documentation required for NDAs runs into

thousands of pages (100,000 plus) of test results and analysis, which takes time for a panel of experts to sieve through. The hard fact is that for FDA applications, the success rate is only 27% of NDA applications and, therefore, uncertainty resolution is not negated at the application stage.

6.1. Shareholder wealth effects: FDA applications and approvals

Table 2 reports shareholder wealth effects for the sample of firms listed on the NYSE (Panel A) and the LSE (Panel B) announcing an application of, or filing, a new drug application (NDA) to the FDA. The market reaction on the event day 0 for NYSE listed firms is 0.28% and is statistically insignificant. However, the run-up to the application announcement experiences significant positive abnormal returns. The CARs for holding period days (-5:-1) and (-10:-1) are 1.24% and 1.73% respectively, and are statistically significant at the 5% level. The CAR for holding period days (-21:-1) is statistically insignificant, suggesting that the information leakage surrounding application announcements begins approximately ten days before the announcement. This finding supports both $\mathbf{H_1}$ and $\mathbf{H_2}$, providing evidence that NDA applications to the FDA are value-relevant and that there appears to be information leakage leading to significant positive abnormal returns in the run-up to the firm's decision to file an application with the FDA for NYSE listed pharmaceuticals. The results reported in Panel B for UK listed firms are in sharp contrast to those for US firms reported in Panel A. The announcement of NDA filings by UK firms appears to induce no significant abnormal returns over the various holding periods as none of the *t*-statistics for the event day holding period returns are statistically significant.

Shareholder wealth effects for FDA approvals are reported in Table 3. It appears that FDA approval announcements are not subject to information leakage since none of the pre-event period CARs (holding period days -21:-1) are statistically significant for either market. NYSE listed firms experience a significant positive CAR of 1.65% (*t*-statistic 7.90), over holding period days zero to one (0:1) reported in Panel A of Table 3. The CAR for holding period days (2:21) is statistically insignificant, indicating that the market reaction is concentrated on the announcement day and the following day. These results support $\mathbf{H_3}$ and $\mathbf{H_4}$ for NYSE listed stocks: approval announcements are value-relevant and lead to post-event abnormal returns, consistent with the attention-grabbing hypothesis. For NYSE listed stocks, applications to the FDA and approvals by the FDA lead to significant increases in shareholder wealth. For example, the combined application and approval CAR is 3.67%. This is composed of the application CAR of 2.01 (1.73% + 0.28%), reported in Table 2 for holding period days (-10:-1) and Day (0) respectively, plus the approval CAR of 1.65% for holding period days (0:1) reported in Table 3. In contrast, McNamara and Baden-Fuller (2007) report abnormal returns of 6.38% on announcement day 0 for their sample of 84 new drug approvals.

INSERT TABLES 2 AND 3 ABOUT HERE

Again we find support for $\mathbf{H_3}$ and $\mathbf{H_4}$ for LSE listed stocks reported in Table 3 for post event days 1 and 2 but not on day 0; it would appear that FDA announcements are made when the London market is closed, and thus the first opportunity for the London market to react is day 1. On day 1, LSE listed stocks experience a significant positive abnormal return of 0.78% (*t*-stat 3.57), and 0.48% (*t*-stat 2.20) the next day, with the CAR (1:2) at 1.27% *(t*-stat 2.88). Similar to NYSE listed firms, the post-event CAR (3:21) for LSE listed firms, which excludes the immediate effects of the announcement over the first two days, is statistically insignificant. It is only if we include days 1 and 2 that the post-event CAR (1:21) reported in Panel B in Table 3 is close to statistical significance at about the 0.05 level (i.e. *t*-statistics of 1.94 against a normal 1.96 for 5% level statistical significance). It appears, therefore, that the investor base for NYSE listed firms capitalises R&D expenditure earlier in the drug development process than LSE listed pharmaceuticals. Our findings are consistent with Dedman et al. (2008), in that they confirm their conclusion that investors in LSE listed stocks capitalise R&D expenditure in the later stages of the drug development process. Dedman et al. report a significant mean abnormal return of 0.79% on day 0, with a three-day CAR of 1.10%; we have 0.78% and a two-day CAR of 1.27% for approvals. The similarity of these results has at least two implications. Firstly, the magnitude of wealth effects for UK firms at the approval stage has approximately the same economic benefit as it does for US firm when approval is granted by the FDA. Secondly, it appears that the economic benefits at the exploitation stage of R&D to investors in UK listed firms have remained relatively constant over time. However, for a like-for-like comparison with Dedman et al.'s findings, we would need a sample of UK Medicines Control Agency approvals up to the end of our sample period. Nonetheless, our findings provide important updated insights for a range of

stakeholders. Given the dearth of pharmaceutical sector-specific research, there is considerable scope for further research.

6.2. Shareholder wealth effects: enhanced drugs and new molecular entities

Our analysis of the market reaction to applications, conditional upon whether they are new molecular entities or enhancements to existing drugs, is reported in Table 4. Consistent with our earlier finding for applications for LSE listed firms, no mean or cumulative abnormal returns are statistically significant. However, when we examine the results for NYSE listed

INSERT TABLE 4 ABOUT HERE

firms, an interesting picture emerges which helps to explain our earlier results for overall applications. As reported in Table 2, whilst the mean abnormal return for NYSE listed firms' FDA applications on day 0 is 0.28% and is statistically insignificant, the pre-event CAR (-5:0) of 1.52% is significant at 1% level. When the data is partitioned into new and enhanced drugs applications as reported in Table 4, for NYSE listed firms, the pre-event day CARs are only statistically significant for enhanced drug applications. None of the holding period day CARs is statistically significant for Panel A in Table 4 for NYSE new drug applications. Therefore, it would appear that the results reported in Table 2 regarding the statistical significance of pre-event day CARs are driven by enhanced drug applications. Significantly, in Table 4, the CARs for holding period days (-5:0) for enhanced drug applications is 1.72% (robust *p*-value 0.001). This supports $\mathbf{H_1}$ and $\mathbf{H_2}$ for NYSE listed firms, but, importantly, identifies the source of the market reaction. Consequently, the differing market reactions between applications for new drug approvals and enhancements to existing drugs provide

evidence to support $\mathbf{H_5}$ at the application stage. Indeed, the shareholder gains surrounding application announcements appear to be driven by drug enhancements.

INSERT TABLE 5 ABOUT HERE

The equivalent results for drug approval announcements are reported in Table 5. Again, there is no evidence of information leakage before announcement of approvals, as none of the pre-event CARs is significant for either market or type of approval announcement. NYSE listed stocks experience statistically significant abnormal returns for approvals of new and enhanced drugs at, and immediately after, announcement. On the announcement day, NYSE listed stocks experience a mean abnormal return of 0.84% (*p*-value 0.001), and 1.95% (*p*-value 0.001) for the following day, with a CAR (0:1) of 2.79% (*p*-value 0.001). The equivalent results for approval of enhanced drugs are 0.44% (*p*-value 0.012), 0.52% (*p*-value 0.004) and 0.96% (*p*-value 0.001) for the two-day CAR. This finding provides additional support for $\mathbf{H_3}$, $\mathbf{H_4}$ and $\mathbf{H_5}$ for the NYSE sample, and confirms $\mathbf{H_3}$, that approvals are value-relevant, and that this result holds, irrespective of whether the approval is for completely new molecular entities or enhancements to existing drugs. The significant mean abnormal return on the day following an approval (day 1) supports the attention-grabbing hypothesis, $\mathbf{H_4}$. However, it does appear that investor attention is magnified for new drug approvals. The market reaction on day 1 is 2.75 times higher (1.95/0.52) than on the announcement day for enhanced drug approvals. When we compare the two-day CARs, their magnitude does suggest (2.79% versus 0.96%) that the market discriminates between the type of drug approval, and that new drug approvals are valued more highly by investors on the NYSE.

From a real-options perspective, however, it does highlight the value created by additional options created from an initial R&D investment.

For LSE listed stocks, new and enhanced drug approvals, as reported in Table 5, significantly increase shareholder wealth. New drugs have a day 1 mean abnormal return of 0.67% (*p*-value 0.032) with a two-day CAR (1:2) of 1.02% (*p*-value 0.026). For enhanced drug approvals, the day 1 mean abnormal return is 0.96% (*p*-value 0.001), day 2 is 0.45% (*p*-value 0.056) and the two-day CAR (1:2) is 1.41% (*p*-value 0.001). The combined total CARs for holding period days (0:1) for LSE is 1.34% (0.38% + 0.96) whilst the equivalent for NYSE is 0.96% (0.44% + 0.52%). Our reported results suggest that the follow-on options for the firms in our study appeared to be valued higher for firms listed on LSE than NYSE. This finding also suggests that the follow-on options created from initial investments have a greater impact on shareholder wealth than new announcements for LSE listed firms. There appears to be the need for a further study to examine the market valuation of follow-on options, particularly on how the market incorporates such information into the valuation process.

7. Conclusion

Non-financial performance indicators have been shown to significantly impact on firm value in intangibles-intensive industries. In the pharmaceuticals sector, outcomes from R&D are a key performance indicator, with empirical evidence showing positive drug-in-progress announcements to be value-relevant. In this paper, we evaluate shareholder wealth effects at the exploitation stage for firms listed on the LSE and NYSE seeking regulatory approval from the United States' Food and Drug Administration (FDA).

We empirically test the value relevance of applications to the FDA, and subsequent approvals by the FDA, of completely new drugs and enhancements to existing drugs. Furthermore, we focus our attention on the pre-event period to investigate information leakage, and the post-event period to evaluate the contribution of mean abnormal returns after an announcement. We find that only NYSE listed firms' application announcements lead to significant positive abnormal returns that are driven by applications to the FDA for approvals of enhancements to existing drugs. We also find significant positive cumulative abnormal returns prior to the submission of an application; this implies information leakage. For LSE listed firms, investors do not appear to value R&D expenditure at the application stage. The heterogeneity in the market's reaction across markets and type of event provides important empirical evidence in the context of the extant literature. The analysis of pharmaceuticals listed on the London Stock Exchange by Dedman et al. (2008) was in-part motivated by the need to provide UK specific evidence. We emphasized at the outset that evaluating shareholder wealth effects for firms listed on both markets, applying to the same regulator at the same stages of the drug approval process effectively held these parameters constant. Our comparative analysis confirms, and quantifies, that the market's reaction to equivalent events are economically and statistically different. An important extension of this line of enquiry would be to explain why the market's reaction differs. The evidence we provide of information leakage prior to NYSE applications for enhanced drugs may be of interest to regulators who are responsible for maintaining market integrity.

We do not find any evidence in the pre-event period of information leakage related to FDA approval announcements in either market. Economically and statistically significant positive abnormal returns are realised on the day immediately following the event day in the

post-event period. These returns contribute to significant two-day cumulative abnormal returns for NYSE and LSE listed firms. This result demonstrates the value relevance of approvals, and supports the attention-grabbing hypothesis proposed by Barber and Odean (2008). Their model emphasises the role of individual investors in driving returns the day after a major news announcements. While our results are consistent with the predictions of this model, a potentially important contribution would be to establish a causal link between the trading behaviour of individual investors and shareholder wealth effects the day after FDA approval announcements. Lack of access to appropriate data to directly test this proposition is a limitation of this paper, and obvious obstacle which, if overcome, has the potential to offer new insights from a behavioural finance perspective which would be new to this literature.

Our analysis indicates that the market reaction to new drug approvals is greater than approvals of enhancements for NYSE firms, whereas the opposite is the case for the real options created from initial R&D expenditures for LSE listed firms. We find that applications to the FDA for drug approvals significantly increase shareholder wealth for NYSE firms only and are driven by applications for enhancements to existing drugs, which appear to be susceptible to information leakage. FDA approvals significantly increase shareholder wealth both for LSE and NYSE firms, with economically and statistically significant two-day cumulative abnormal returns (CARs) of 1.27% and 1.65%, respectively. Examination of approvals by type indicates that the market discriminates between enhanced versus new drug approvals. New drug approvals for NYSE firms earn two-day CARs of 2.79%, while for enhanced drugs it is 0.96%. For LSE listed firms, the equivalent CARs are 1.02% and 1.41%. Drug-in-progress announcements are undoubtedly major news items for

pharmaceuticals firms. The fact that a large proportion of the two-day CARs emanate from a significant market reaction on the day immediately after the event day supports the attention-grabbing hypothesis and highlights the importance of news and extreme one-day returns in grabbing individual investors' attention (Barber & Odean, 2008).

This finding supports the contention that the market differentiates between types of drug approval and that follow-on options are an important determinant of firm value. By distinguishing between new and enhanced drug applications to the FDA, we are able to attribute the significant market reaction to applications for NYSE firms to enhanced drug applications. In economic terms, significant increases in shareholder wealth surrounding applications and approvals of enhanced drugs highlights the importance of real (follow-on) options in creating wealth in the pharmaceutical industry.

A significant contribution of this study to the real-options literature is that it objectively quantifies the market value of follow-on options irrespective of managers' understanding of, and their ability to implement it systematically as an investment appraisal technique. A significant proportion of this literature has focused on the extent to which decision makers' intuition is consistent with real-option theory (Busby & Pitts, 1997; Howell & Jägle, 1997; Remer, Ang & Baden-Fuller, 2001; Verbeeten, 2006) and there is general agreement that biotechnology/pharmaceuticals firms' market value can be considered as the value of a basket of real options on their R&D portfolio (Ely et al., 2003; Woerner & Grupp, 2003; Hartman & Hassan, 2006). A theme is this literature is a call for better educated decision makers to realise the benefits of the real-options approach for investment appraisal. Our analysis shows that there are real economic benefits to real-options. Consequently, this should provide an incentive to firms to ensure that their key decision makers understand

when they are faced with a real-option problem. It might also be in the best interest of firms to introduce a rigorous real-options investment appraisal methodology to aid in the allocation of capital. It is well documented in the literature that there is considerable variation in regards to both. A further implication of the reported results of this study is the need for more empirical evidence on market response to such follow-on options in other sectors of industry.

Our *ex-post* analysis offers one technique for clear identification of follow-on options which have been exercised, and provides an estimate of their market value. This is regardless of whether managers exercising the option employed option-pricing methodology, *ex-ante*, to evaluate the investment opportunity in the form of enhanced drug applications, or understood conceptually that they were executing a follow-on option in the absence of a pricing methodology.

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Notes:

1. Conventional valuation techniques may be applicable for our sample of the largest pharmaceutical firms, as they tend to be sustained by cash-flows from a diversified portfolio of existing products.
2. The 'burn-rate' KPI came into common parlance during the dot-com era. It is a measure of how fast a company will use up its shareholder capital. If the shareholder capital is exhausted, the company will either have to start making a profit, find additional funding or close down.
3. The Code can be downloaded from the Bio-industry website at: http://www.bioindustry.org/
4. McNamara & Baden-Fuller (2007) identify six micro-stages: patenting, pre-clinical trials, the three human clinical trial stages, and application and approval of the NDA to the FDA. We distinguish between application and approval and refer to each stage individually in subsequent empirical analysis. Instead, we have Stage 4 as application, while approval is Stage 5. We group human clinical trials into Stage 4 with three phases, I, II and III
5. We provide a brief overview of the drug development process, as it has been discussed in detail in the literature. See Dedman et al. (2008), McNamara & Baden-Fuller (2007) and Sarkar & de Jong (2006) for detailed expositions of the approval processes and historical development of the Medicines Control Agency in the UK and the Food and Drug Administration in the US.
6. It is beyond the scope of this paper to cover the extensive disclosure literature. Given our focus on the impact on shareholder wealth from disclosing non-financial indicators specifically related to the drug development process, our literature survey elucidates evidence mostly from event studies. See Hail et al. (2009) for a review of the disclosure literature.
7. Dedman et al. (2008) initially identify 27 categories in the UK's Medicines Control Agency's drug development process, which they then combine into 17 incremental stages. The 17 stages are then grouped into two samples: early stage (exploration) and later stage (exploitation) announcements. In our analysis, applications and approvals are equivalent to announcement types N and Q in their classification.
8. Successful phase III trials in the UK increase the odds of a drug making it to market to more than 75%. In the US, commencement of phase II trials has a final success probability of 30%; success of phase II increases final success probability to 60%; successful phase III increases the probability of final success to over 70% (Dedman et al., 2008).
9. Barber and Odean (2008) employ three proxies for attention: news, trading volume and extreme one-day returns. In their study, they examine the day following extreme returns to mitigate endogeneity. In an event study context, strict application of the model implies possible post-event abnormal returns on day +1. They point out that news items such as FDA approvals will catch the attention of some investors, while the extreme one-day returns will catch the attention of others (the previous day's big gainers and losers, which even becomes the news itself in the absence of news), and that many investors may learn of and/or react to the extreme returns/news after the market closes, and their first opportunity to respond is the next trading day.
10. One of the most commonly known examples of a drug found to have alternative uses is Viagra™. Originally it was developed by Pfizer to treat angina. Its ability to treat erectile dysfunction opens up an entirely new market with estimated annual sales of approximately £1 billion per year.
11. Brown & Warner (1985) describe the market model as being both well specified and relatively powerful under a wide variety of conditions. MacKinlay (1997) points out that the marginal benefits from employing more sophisticated multi-factor derivations of the market model are empirically small, as evidenced by the limited increase in additional explanatory power. Also, we employ the robust variance estimator reported in Hamill et al. (2002) when computing cumulative abnormal returns, which simultaneously accounts for misspecification of the market model. Adopting the market model allows us to utilise this estimator and make comparisons with the robust *p*-values we also generate for mean abnormal returns using Corrado's

(1989) non-parametric rank test. The benefits of employing multi-factor models tend to materialise over a longer time period, typically years (Fama, 1993; Fama & French, 1996).

12. As no new econometric techniques are introduced in the paper, the aim of the methodology section is to outline the approach taken and the key tests employed. For an extensive treatment of the tests employed here, see Hamill et al. (2002) and references contained therein.
13. An earlier version of this paper included an analysis of value implications of filings to the European Medicines Agency. Given the fact that nearly all applications for marketing approval to the EMEA are filed after approval from the FDA, no significant value implications are found in our earlier analysis. We have removed the analysis from this version of the paper, but results and data can be obtained from the authors.

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Table 1 Food and Drug Administration Regulatory Notifications Sample

Year	Applications		Approvals	
	NYSE	LSE	NYSE	LSE
1991	-	2	-	0
1992	-	1	-	12
1993	-	3	-	3
1994	-	4	-	9
1995	-	10	-	18
1996	-	9	-	9
1997	-	9	-	16
1998	1	15	-	12
1999	-	12	-	9
2000	9	6	-	8
2001	8	8	-	9
2002	14	8	1	5
2003	40	1	-	8
2004	40	0	45	4
2005	46	2	52	1
2006	40	1	61	1
2007	17	0	46	1
2008	0	0	4	0
Total	**215**	**91**	**209**	**124**

Notes: NYSE is New York Stock Exchange; LSE is London Stock Exchange

Table 2
Shareholder wealth effects: FDA Application Announcements

Event Days	*Abnormal Returns (%)*	*t-statistic*	*Robust p-values*	*Proportion of Positive Abnormal Returns (%)*
		Panel A: NYSE Listed		
[-21, -1]	1.22	1.60	0.087	48
[-10, -1]	1.73	1.96 *	0.002**	50
[-5, -1]	1.24	2.03 **	0.002**	50
[-5, 0]	1.52	3.70 **	0.001**	49
0	0.28	1.66	0.774	50
1	-0.18	-1.08	0.305	41
2	0.01	0.06	0.480	50
[1, 2]	-0.16	-0.49	0.532	47
[1, 21]	0.47	0.60	0.302	51
[2, 21]	0.65	0.51	0.232	49
[3, 21]	0.64	0.51	0.231	49
		Panel B: LSE Listed		
[-21, -1]	-1.96	-1.23	0.217	50
[-10, -1]	-1.49	-1.35	0.147	43
[-5, -1]	-1.36	-1.77	0.052	39
[-5, 0]	-1.36	-1.61	0.079	41
0	0.01	0.01	0.381	39
1	0.09	0.29	0.206	39
2	-0.10	-0.35	0.720	60
[1, 2]	-0.01	-0.03	0.970	62
[1, 21]	-0.88	-0.35	0.590	51
[2, 21]	-0.97	-0.40	0.530	50
[3, 21]	-0.86	-0.37	0.573	50

Notes:
The sample consists of 91 UK and 215 US listed pharmaceutical companies announcements of FDA application filings from January 1992 to December 2008. * *significant at* 0.05 level; ** *significant at* 0.01 level

Table 3
Shareholder Wealth Effects: FDA Approval Announcements

Event Days	*Abnormal Returns (%)*	*t-statistic*	*Robust p-values*	*Proportion of Positive Abnormal Returns (%)*
		Panel A: NYSE Listed		
[-21, -1]	0.06	0.09	0.411	50
[-10, -1]	0.16	0.20	0.304	46
[-5, -1]	0.17	0.20	0.245	49
[-5, 0]	0.61	1.00	0.050*	51
[0, 1]	1.65	7.90 **	0.001**	59
0	0.44	2.90 **	0.003**	55
1	1.20	7.89 **	0.001**	56
2	0.07	0.44	0.375	46
[1, 2]	1.27	4.16 **	0.001**	53
[1, 21]	0.74	0.62	0.141	50
[2, 21]	-0.49	-0.76	0.530	49
[3, 21]	-0.53	-0.46	0.443	49
		Panel B: LSE Listed		
[-21, -1]	-0.48	-0.39	0.775	54
[-10, -1]	-0.31	-0.26	0.690	48
[-5, 0]	-0.69	-0.80	0.232	49
[-5, -1]	-0.64	-0.81	0.222	51
[0, 1]	0.73	1.67	0.013*	55
0	-0.06	-0.25	0.605	47
1	0.78	3.57**	0.001**	62
2	0.48	2.20**	0.001**	60
[1, 2]	1.27	2.88**	0.001**	63
[1, 21]	2.35	1.94	0.079	60
[2, 21]	1.56	0.93	0.097	50
[3, 21]	1.09	0.68	0.239	48

Notes:
The sample consists of 124 UK and 212 US listed pharmaceuticals announcements of FDA approval from January 1992 to December 2008. * *significant at* 0.05 level; ** *significant at* 0.01 level

Table 4

Shareholder Wealth Effects: New versus Enhanced FDA Applications

Event Days	*Abnormal Returns (%)*	*Robust p-values*	*Abnormal Returns (%)*	*Robust p-values*
	Panel A: New drug applications			
	NYSE		LSE	
[-21, -1]	-0.09	0.957	-3.34	0.158
[-10, -1]	1.26	0.160	-1.33	0.371
[-5, -1]	0.92	0.149	-0.88	0.382
[-5, 0]	0.99	0.153	-0.79	0.476
[0, 1]	-0.38	0.491	0.05	0.465
0	0.07	0.432	0.09	0.421
1	-0.45	0.254	-0.03	0.939
2	-0.03	0.943	0.19	0.332
[1, 2]	-0.48	0.393	0.15	0.401
[1, 21]	-2.57	0.162	-1.75	0.459
[2, 21]	-2.21	0.251	-1.71	0.428
[3, 21]	-2.09	0.249	-1.90	0.390
	Panel B: Enhanced drug applications			
[-21, -1]	1.65	0.058	-0.06	0.981
[-10, -1]	1.77	0.005**	-0.95	0.550
[-5, -1]	1.42	0.001**	-1.11	0.279
[-5, 0]	1.72	0.001**	-1.18	0.306
[0, 1]	0.20	0.265	-0.04	0.939
0	0.29	0.095	-0.07	0.879
1	-0.09	0.674	0.02	0.482
2	0.05	0.408	-0.15	0.737
[1, 2]	-0.04	0.894	-0.13	0.837
[1, 21]	1.18	0.134	1.83	0.212
[2, 21]	1.26	0.109	1.81	0.205
[3, 21]	1.22	0.113	1.97	0.182

Notes:

The sample consists of 56 (61) new and 151 (60) not new NYSE (LSE) listed pharmaceuticals announcements of FDA applications from January 1992 to December 2008 (2008)..

* *significant at* 0.05 level; ** *significant at* 0.01 level

Table 5

Shareholder Wealth Effects: New versus Enhanced FDA Approvals

Event Days	*Abnormal Returns (%)*	*Robust p-values*	*Abnormal Returns (%)*	*Robust p-values*
	Panel A: New drug approvals			
	NYSE		LSE	
[-21, -1]	-1.11	0.354	1.45	0.234
[-10, -1]	-0.13	0.821	0.55	0.325
[-5,-1]	-0.02	0.496	-0.52	0.539
[-5, 0]	1.29	0.025*	-0.95	0.310
[0,1]	2.79	0.001**	0.24	0.323
0	0.84	0.001**	-0.44	0.233
1	1.95	0.001**	0.67	0.032*
2	-0.02	0.945	0.34	0.173
[1, 2]	1.93	0.001**	1.02	0.026*
[1, 21]	1.81	0.070	3.62	0.040*
[2, 21]	-0.14	0.912	2.94	0.057
[3, 21]	-0.12	0.919	2.60	0.088
	Panel B: Enhanced drug approvals			
[-21, -1]	0.02	0.482	-1.25	0.379
[-10, -1]	-0.13	0.821	-0.63	0.497
[-5,-1]	0.02	0.962	0.50	0.434
[-5, 0]	0.42	0.189	-0.12	0.865
[0,1]	0.96	0.001**	1.34	0.001**
0	0.44	0.012*	0.38	0.088
1	0.52	0.004*	0.96	0.001**
2	-0.33	0.094	0.45	0.056
[1, 2]	0.19	0.246	1.41	0.001**
[1, 21]	-0.66	0.431	0.60	0.335
[2, 21]	-1.18	0.151	-0.36	0.790
[3, 21]	-0.85	0.293	-0.82	0.539

Notes:

The sample consists of 54 (61) new and 145 (60) enhanced NYSE (LSE) listed FDA applications announcements from January 1992 to December 2008 (2007). * *significant at* 0.05 level; ** *significant at* 0.01 level