

# Discussion—“The Usefulness of Biotechnology Firms’ Drug Development Status in the Evaluation of Research and Development Costs”

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## 1. Introduction

Ely, Simko, and Thomas (hereafter, EST) examine the usefulness to investors of drug development information disclosed by start-up biotechnology firms with no marketable products. Drug research is a highly standardized multistage process monitored by the Food and Drug Administration. Providing information on intermediate R&D results might resolve investors’ uncertainty about a firm’s ability to generate future revenues from particular R&D projects, and might therefore affect their firm value assessment. EST find that clinical trial disclosures help investors assess the uncertainty of in-process drugs’ revenue potential, and that there exists a specific drug development stage at which investors start to treat R&D costs as probable future revenue-generating assets. I discuss the relevance and motivation of the research topic, the authors’ research design choices, the validity of the results, and future research.

## 2. Relevance and Motivation of the Research

The motivation for the study stems from the Jenkins Committee report that promotes the disclosure of additional nonfinancial (forward-looking) information and from the current concern that recognized financial statement numbers are less value-relevant for R&D intensive firms. On January 9, 2002, the FASB added a new project to its agenda to address disclosure of information about internally developed intangible assets. Disclosures on clinical trial outcomes could be considered as what the FASB project calls “significant events that change the anticipated future benefits arising from intangible assets” (FASB [2002]). The underlying intangible asset in drug research is the R&D capital obtained by successful R&D investments. The current interest of both the investment community and the accounting standard setter in additional disclosures about investments in intangibles makes the EST study very relevant. The above-mentioned motivation of the paper

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raises three issues, one is the disclosure process in the biotech industry, another relates to policy implications, and a third issue focuses on the generalizability of the findings.

First, since ETS examine the usefulness and valuation implication of development stage data, it is appropriate to discuss what and how information about a biotech firm's R&D activities is disclosed to the investment community. Standard setters might be especially interested in targeting that phase in the R&D process where information asymmetry between the firm and the investment community is largest. Given the long R&D cycle to develop a drug (13 to 15 years), uncertainty about R&D success is resolved at various points in the process, and often through other sources than company announcements. I discuss the various R&D stages and how investors obtain information about the R&D outcomes in these stages.

Discovery drug research and preclinical testing results are often published in scientific journals. Halperin and Chakrabarti (1987) find that the number of pre-clinical publications is highly correlated with the presence of "elite" scientists, who are part of a firm's knowledge or R&D capital. Results from basic research and preclinical drug tests are also reflected in the number of patents filed to the U.S. Patent Office. Joos (2002) finds that the number of patent applications significantly affects the market valuation of R&D of pharmaceutical firms. Both scientific publications and patents are early indicators of R&D success. Companies only sporadically disclose preclinical research and patent approvals in their financial statements. Alternative sources such as the U.S. Patent Office and academic journals provide more comprehensive, more detailed and more timely information on early R&D capabilities.

EST examine information on clinical trials, and rely on annual survey information provided by the American Association of Pharmaceutical Manufacturers (PhRMA). Analyst reports, company announcements, conference abstracts and medical journal articles are alternative information sources on clinical trials. These information sources are the input for commercial R&D pipeline databases such as Pharmaprojects of PJB Publications, R&D Focus of IMS Global Services, or R&D Insight of ADIS International (Mullen et al. [1997]). Clinical trial results sometimes reach investors before companies' press releases. Arnst (2002) indicates the importance of professional meetings, such as the meeting of the American Society of Clinical Oncology, as important sources of information. Abstracts on clinical trial results are typically made available exclusively to members of these societies a few weeks before the meeting. Although there is no legal restriction, firms typically do not comment on abstracts before the meeting. However, nothing prevents physicians from trading on that information or from passing it to financial analysts. In June 2002, PhRMA released a new set of principles to conduct clinical trials and communicate the results of these investigations to the public. If clinical trials involve products that are already approved (phase IV clinical trials), then firms should communicate these results in a timely manner through peer-reviewed medical journals, abstracts or posters at a scientific meeting, or press releases, regardless of the outcome of the investigation. However, investigational new drug (IND) applications

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and phase I results are often highly proprietary to the company, and therefore PhRMA leaves disclosure of the results in these stages to the company's discretion. Fisher (2002) gives an overview of R&D disclosure practices of pharmaceutical and biotechnology firms, and cites many court cases in which companies misled investors about clinical trials results.

Finally, FDA approval-rejection decisions provide a late stage R&D success indicator. The new drug application (NDA) submission success rates vary between 76 and 86 percent in the period 1980–1995 (DiMasi [2001]). Prior studies focused on final FDA decisions. Shortridge (2001) finds that the stock market values R&D higher for firms with relatively more drug approvals. Torabzadeh et al. (1998) find the share price response to positive and negative FDA decisions is asymmetrical; the market reaction to rejections or deferrals of NDAs is of greater magnitude than that for positive decisions. However, the ultimate R&D success is reflected in drug sales after FDA approval. Uncertainty about the R&D benefits is gradually resolved by the drug's sales pattern over time and the firm's changing therapeutic market shares. Analyst reports, the IMS Health database, and company disclosures provide information on drug revenues and therapeutic market shares.

To summarize, uncertainty about future benefits from R&D investments is resolved at various stages in the R&D process and communicated to the investment community through various information channels. Annual and quarterly reports only provide a small fraction of information on the R&D pipeline. EST focus on the clinical trial stages and rely on self-reported clinical trial results for their empirical analysis. However, the finding of a significant correlation between the number of drugs in a specific stage and market value of equity has no immediate financial reporting implication as to whether firms should disclose drug pipeline information more comprehensively in their annual reports, since the stock market already values the pipeline information from other data sources.

The second issue in this section focuses on the policy implications of the EST study. EST find their results useful as a starting point in regulatory deliberations, even though they do not recommend a specific capitalization method or indicate how companies should disclose outcomes of clinical trials. In particular, EST claim to provide evidence on “perceived” *technological feasibility* in a specific drug development stage, in particular phase II (Ph2). Technological feasibility is used as a criterion to capitalize software development costs. However, the analogy with the capitalization argument in the software industry is not completely accurate, since technological feasibility is only satisfied after all planning, designing, coding, and testing activities have been completed. Aboody and Lev (1998) provide evidence that only a small portion—typically less than 25 percent—of the total software development costs does get capitalized, and that capitalization only occurs in very late stages of the development process. However, biotech R&D expenses during and after the clinical trials comprise more than 50 percent of the total R&D investments (PhRMA [1999]). EST base their main conclusions on a traditional value relevance methodology. Apart from the self-reporting bias in clinical tests (especially in early stages) discussed above, the methodology used by EST does not

allow us to make any policy recommendations. Holthausen and Watts (2001) and Ronen (2001) provide an excellent discussion on the problems with the value relevance methodology. Briefly, one cannot assess the usefulness of accounting and nonaccounting information (e.g., drug counts) solely by means of association with market prices or market returns. For example, would capitalization of R&D investments at a specific stage generate “better” or “more socially desirable” earnings numbers? What would be the social objective function to evaluate different accounting treatments of R&D? Healy et al.’s (2002) simulation methodology is much more suitable for policy recommendations on R&D accounting treatments. Also, would it be more desirable to require companies to disclose more R&D pipeline information in their financial reports, in addition to press releases, scientific journal articles, patent information, conference abstracts and posters? Would financial reports become more useful?

The third issue relates to the generalizability of the EST findings. In particular, what do accounting researchers learn from the study other than expanding their knowledge on pure-play biotechnology start-up companies? Would the findings also hold for mature biotechnology and pharmaceutical companies, such as Amgen and Merck? If not, how and why would the value relevance of the R&D pipeline differ from that of the EST sample firms? Also, what about the applicability of the EST findings to other high-technology start-ups, such as computer firms, software firms, or some R&D intensive Internet firms? An answer to these questions would make the EST study more interesting to accounting researchers.

### 3. Research Design

#### 3.1 Sample

EST examine the market valuation of nonfinancial information (in essence drug counts in different development stages) in a sample of biotechnology start-up companies with no approved drugs. A thorough understanding of the sample composition is key in interpreting the empirical findings. I discuss three sampling issues that possibly affect the estimation results.

First, the sample is constructed from eight annual PhRMA surveys in the period 1988–1998 and resulted in 83 unique “pure-play biotechnology” firms (193 firm-year observations). The average age of these firms is 9.9 years. Based on the success probabilities reported in the article (Ph1 5%, 8% Ph2, 11% Ph3, and 50% AS), I computed the following proportions of drugs in each phase: 45 percent in Ph1, 29 percent in Ph2, 21 percent in Ph3, and 4.5 percent in AS.<sup>1</sup> These proportions differ from the reported sample proportions in Table 2: 34 percent (1.01/3.00) in Ph1, 42 percent (1.26/3.00) in Ph2, 18 percent (0.54/3.00) in Ph3, and 6 percent

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1. If 100 drugs enter Ph1, then 65 are expected to enter Ph2 ( $13/20 \times 100$ ), 46 of these drugs are expected to enter Ph3 ( $9/13 \times 100$ ), 10 of these drugs enter AS ( $2/9 \times 100$ ) and 5 are expected to be eventually approved by the FDA ( $1/2 \times 100$ ).

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(0.19/3.00) in AS. The sample shows a disproportionately large number of drugs in Ph2, exactly that phase in which EST claim to find significant market valuation effects of R&D costs. One reason for the oversampling of Ph2 drugs might be a reporting bias in the PhRMA surveys with firms underreporting Ph1 clinical trials. Biotechnology firms might not want to disclose the existence of Ph1 clinical trials for competitive reasons. For example, disclosure of early R&D results might attract the attention of large pharmaceutical or other biotechnology firms and jeopardize the R&D program. Misakian and Bero (1998) discuss the reporting bias against publishing negative clinical trial results in medical journal articles. Since the majority of Ph1 trials result in negative findings (i.e., no proof of a therapeutic effect), most of these trials are never reported in the academic literature, and therefore never reach the investment community. However, it is much more difficult to hide Ph2 and Ph3 clinical trials given the involvement of a large number of patients and doctors in these phases. Even though the FDA monitors the R&D process, the FDA never discloses IND applications or clinical trial results, nor does it report rejected new biopharmaceutical entity applications (AS drugs). An alternative explanation for the oversampling of Ph2 drugs is a potential decline in early stage R&D projects for the sample firms, resulting in a lower than expected number of early clinical trials (Ph1). This sampling feature might bias the estimation results in favor of finding more significant valuation effects on later stage drug development, since early drug stages are underrepresented due to the self-reporting bias (or publication bias).

In addition to the Ph2 oversampling problem, another sampling issue relates to the particular nature of 83 sample firms. Successful biotech firms are often acquired by large pharmaceutical drug manufacturers. Biotech firms with drugs moving to Ph3 or FDA approval stage often can not support the huge costs of Ph3 trials or the marketing expenses and distribution costs to commercialize their drug. Not surprisingly, about half of the 83 sample firms have no drugs in Ph3. The average market size of a control sample firm with at least one approved drug is 10 times larger than the size of the main sample firm without approved drugs. The 14 control pure-play biotech firms with approved drugs are not acquired by traditional pharmaceutical firms and are able to support their own late stage clinical trials and commercialization. I argue that the final sample consists of a disproportionately larger fraction of not yet acquired firms with successful early clinical trials (Ph1 and Ph2) and a set of nonacquired firms with drugs in Ph3 and AS. One reason why the latter set of firms remain independent is that their Ph3 and AS drugs are not commercially promising enough. This sampling feature might bias the tests against finding significant valuation effects in Ph3 and AS.

The last sampling issue relates to the independence of the firm-year observations. Only 34 out of 83 firms appear only once (one year) in the final sample. The majority of the 193 firm-year observations that are used in the regression analyses are not independent, possibly resulting in understated standard errors of the regression coefficients.

### 3.2 Hypothesis Test

The main hypothesis states that R&D costs can explain more variations in equity value for firms with greater drug portfolio potential as opposed to firms with lower drug portfolio potential. To test the hypothesis, ETS spell out a valuation model to relate R&D to market value, and then provide an empirical measure of drug portfolio potential.

The valuation model in eq. (1) relates market value of equity to book value of equity, earnings before R&D expense, R&D expense, firm age, and the number of drugs in each development stage (clinical trials and application). Since ETS provide no theoretical motivation for the use this model, it is not clear why the chosen valuation relation is appropriate to explain the value of biotechnology start-up companies. If the purpose of EST is only to correlate financial and nonfinancial variables with market value of equity, then it is not clear why net income, book value of equity, and R&D expense are the only appropriate financial variables to include in the regression model. For example, Hand (2001) uses a model to value biotechnology companies that includes other financial reporting variables, such as cost of sales, R&D growth, and number of employees.

Alternatively, one could use a more structural model to value biotechnology start-up firms. For example, Darby et al. (1999) provide an option-based pricing model to value new biotechnology firms. They develop an endogenous jump-diffusion model for valuing intellectual human capital (intangible capital) by examining the effect of ties to star scientists on the market value of new biotechnology companies. EST claim that real options or investment flexibility is not an important issue in the clinical trials and FDA submission stages, and therefore expect the value of real options to be low in these R&D stages. Copeland and Antikarov (2001) provide an extensive example of managerial flexibilities in the clinical trials and FDA submission stages. Typically, companies might abandon, defer, scale back, or expand clinical testing investments based on the expected commercial success of its tested drug indications. As noted by EST, a drug might have more than one drug indication or therapeutic use, and FDA approval of all the company's claimed indications often depends on extensive bargaining between the FDA and the company. That is, in order to obtain approval for an additional indication, the company might need to make additional R&D investments to prove the effectiveness of the drug for that specific indication. However, the company has the option to abandon specific R&D investments and accept a more limited set of approvable drug indications.

The second issue in testing the main hypothesis is the proxy for drug portfolio revenue-generating potential. EST use drug counts in eq. (2) as their operational measure for revenue-generating potential. Grabowski and Vernon (1994) show that the revenue distribution of approved drugs is highly skewed, with only 20 percent of the approved drugs generating enough revenues to cover the after-tax R&D investments. Financial analysts typically start to mention the market potential of a drug as it enters late stage clinical trial tests or the FDA submission stage. A simple

count variable, weighted by industry-wide approval probabilities in each stage and scaled by past R&D investments, is a very crude measure of portfolio potential since it assumes all drugs in a stage to have the same revenue-generating potential. EST acknowledge the limitations of their portfolio potential measure, and correctly interpret PORTWGHT as a simple and objective measure of R&D success, similar to Joos (2002), who divides the number of patents by past R&D investments as a measure of early R&D success. Consistent with the findings of Joos (2002) who focuses on success in the preclinical trial stage and Shortridge (2001) who focuses on drug approvals, EST find that companies with higher ex post R&D success in the clinical trials have higher valued R&D, as opposed to companies with lower R&D success. The fact that the stock market only values successful drug development is the key finding in the paper.

### 3.3. Event Study

EST conduct an event study to show the existence of a specific R&D stage at which R&D costs begin implying material expected revenue generating ability. They look at short-window price reactions to announcements about phase initiations or status updates (negative and positive news) and find the most significant reaction to Ph2 initiation and Ph2 status update announcements. Notice how the earlier mentioned publication bias affects the proportion of negative versus positive status updates: 13 negative versus 174 positive updates. Fisher (2002) claims that in many cases the tone in announcements of test results is overly optimistic. No significant price reaction is found in Ph3 or FDA submission announcements. EST interpret their findings as evidence that Ph2 is the point at which investors begin to ascribe a lasting future benefit to a drug's development.

Several alternative explanations might explain the event study findings. Not finding a significant market reaction to Ph3 and FDA submission initiations and updates might indicate a wrong event date. Information on these events typically becomes available through alternative information sources (medical journals, conference posters and abstracts, etc.) before companies make announcements. Also, phase initiation announcements are not always good news because firms might start the next clinical tests for a more limited set of indications than initially thought. For that same reason, FDA approvals are not always automatically good news. EST should provide a more comprehensive discussion of the announcement events, and of the managerial discretion in timing and wording of clinical trial announcements.

## 4. Conclusion and Future Research

EST conduct an empirical study that focuses on the value implications of R&D success in clinical trials. The findings suggest that investors value successful R&D more than less successful R&D. The study adds to our knowledge of the usefulness of nonaccounting information to assess the value of intangible capital, in this case R&D capital. I see at least three directions for future research.

First, accounting research might move toward using more sophisticated valuation models, such as real options models, to describe the valuation of high tech or R&D intensive companies. It would be interesting to see how accounting information could be used in these more structural models.

Second, collecting a richer set of micro level data might provide more insight into how R&D contributes to the value of a biotech firm, or of a R&D intensive firm in general.

Henderson and Cockburn (1994), among others, use data at the R&D program level and find that idiosyncratic firm effects account for a very substantial fraction of the variance in research productivity across pharmaceutical firms.

Finally, managerial disclosure practices in R&D intensive industries are not well understood. What are incentives for companies to disclose early R&D results? Can firms provide enough incentives to researchers when R&D findings are not reported in academic journals or at professional meetings? What is the quality of the current annual and quarterly financial reports with respect to the discussion of the R&D pipeline? The EST study is only the start of a long research agenda to answer these questions.

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