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Biotechnology Stock Prices Before Public Announcements: Evidence of Insider Trading?

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ABSTRACT

Background: **Unique financial challenges faced by biotechnology companies developing therapeutics have contributed to the creation of a highly sensitive market, where stock prices are capable of great fluctuation. The potential for significant financial reward and the nature of the scientific review process make this industry susceptible to illegal share trading on nonpublic information. We examined stock prices of biotechnology products before and after announcement of Phase III clinical trial and Food and Drug Administration (FDA) Advisory Panel results for indirect evidence of insider trading.**

Methods: **Biotechnology stock prices were recorded for 98 products undergoing Phase III clinical trials and 49 products undergoing FDA Advisory Panel review between 1990 and 1998. Prices were recorded for 120 consecutive trading days before and after public announcement of these two events. We compared the average change in stock price of successful products ('winners') with unsuccessful products ('losers') before the public announcement of results for both critical events.**

Results: **The difference between average stock price change from 120 to 3 days before public announcement of results of Phase III clinical trial winners (+27%) and losers (−4%) was highly significant (P=0.0007). A similar but nonsignificant difference was observed between the average stock price of winning (+27%) and losing products (+13%) before FDA Advisory Panel review announcements (P=0.25).**

Conclusions: **Our results provide indirect evidence that insider trading may be common in the biotechnology industry. Clinical investigators may wish to consider this issue before participating in any equity position in the biotechnology industry, especially if they are going to perform research for those companies. (J Investig Med 2000;48:118–124) Key Words: biotechnology industry • insider trading • clinical trials • scientific review**

INTRODUCTION

In the late 1970s, the maturation of molecular biological techniques to synthesize potentially therapeutic proteins such as insulin stimulated the growth of the modern biotechnology industry.[1,2] Biotechnology companies face unique challenges on the road to novel product development[1] and differ from traditional pharmaceutical companies in several important ways. The great majority of these enterprises do not generate product revenues; thus, to obtain product Food and Drug Administration (FDA) approval,[3] they are dependent on capital markets to fund the expensive clinical trial process. Because of their limited financial and personnel resources, biotechnology firms are generally narrowly focused and can usually only develop one or a few potential therapeutics. Therefore, the clinical success of each product greatly affects a biotechnology company's ability to raise additional capital from investors.[1]

The potential for substantial financial gain or loss by investors following the release of clinical trial or regulatory review results makes biotechnology stocks susceptible to great fluctuation in value around these pivotal events.[4] Therefore, accurate speculation of clinical trial

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results before public announcement can prove extremely lucrative for investors. By contrast, as pharmaceutical company stock prices are buffered by the large number of established and developing products in their portfolio, individual product clinical trial results usually have a lessened impact on stock price.[1,5]

The process of scientific publication of clinical data has historically made it possible for large numbers of people to know the results of a particular study months to days before public announcement.[4–10] The use of such information for the purpose of obtaining profit or avoiding financial loss before its public dissemination qualifies as insider trading.[5,11]

The rapidly growing number of products under development in the biotechnology industry may increase the opportunities for illegal trading using valuable, nonpublic scientific information. In this study we retrospectively examined the stock prices of publicly traded biotechnology firms, before and after official announcements of critical results, for indirect evidence of insider trading.

METHODS

Study Question

Our primary question in this study was: is there indirect evidence for insider trading in the biotechnology industry, based on the stock price trends before two critical events: 1) public announcement of Phase III clinical trial results and 2) public announcement of the FDA Advisory Panel reviews. If insider trading is occurring, we might expect to see early positive movement of stock prices in the period leading up to release of critical data to the public for those products destined to be successful. Similarly, we would expect to see a trailing off of stock prices before release of information of those products destined to be unsuccessful.

Study Population

For this study, two groups of well established biotechnology companies with developed products undergoing FDA approval were included in the sample. The group 1 sample consisted of companies whose products (n=98) were undergoing Phase III clinical trials, whereas the group 2 sample included companies whose products (n=49) were undergoing the FDA Advisory Panel review process. Phase III clinical trials are multicentered, randomized controlled trials designed to demonstrate the safety and efficacy of the product. For a product to move toward successful market launch, it must demonstrate a beneficial effect on a prespecified disease endpoint.[3] An appointed Advisory Panel of independent academic experts then meets, following the filing of all accumulated data on a product, to vote in favor of or against recommending approval to the FDA.[3]

A total of 70 biotechnology companies were included in this study. The study sample included every significant biotechnology product in late stage development between 1990 and 1998. The biotechnology products consisted of therapeutic drugs or biologics engineered for therapeutic purposes (a biologic is any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product).[3]

The unit of observation was the company's daily stock price before and after the public announcement of pivotal trial results. Therefore, the same companies could appear twice in the sample. Eighteen of the 49 products in the group 2 sample (37%) appeared earlier as group 1 products undergoing phase III clinical trials. We excluded pharmaceutical companies with multidrug portfolios from this study, as well as products from one prominent biotechnology company. The latter was omitted because the company's majority ownership was a pharmaceutical company, and its remaining publicly traded stock was a putable/callable security with prespecified maximum and minimum prices. (Putable indicates that shareholders had the right to sell to the pharmaceutical compamy at a prespecified price, and callable means that the company had the right to buy at a prespecified price.)

All companies studied are traded on the National Association of Securities Dealers Automated Quotation (NASDAQ) System, the New York Stock Exchange, and the American Stock Exchange. The closing daily stock prices for each company are widely published.

Study Design

We retrospectively examined stock prices of companies before and after the date of announcement of 1) Phase III clinical trial results (group 1) and 2) FDA Advisory Panel approval for market launch (group 2).

Publicized stock prices of the companies were recorded daily for 120 consecutive trading days before and 120 consecutive trading days after the formal announcement of trial results or the announcement of each FDA advisory panel decision. Trading days refers to consecutive dates the market was open for active trading (ie, excluding weekends and statutory holidays); 120 trading days is equivalent to 6 calendar months. We defined 'day −120' as the first recorded trading day in the study and 'day +120' as the last. The 'zero date' was defined as the day before the date that active trading could occur on the news of clinical trial results. If results were reported between trading hours, the announcement date was day zero. If the announcement came during trading hours, the previous day was the zero date. Clinical trial results were reported through a variety of means, including at scientific meetings and in scientific journals, usually with a concurrent press conference release.

Individual stock price changes were calculated from day −120 (ie, the first day of price recording) and compared as a percent change from that point onward. The percent change in the NASDAQ index average was simultaneously recorded at the time of each product's price recording for both groups. These results were averaged for all products to provide a concurrent market reference.

Statistical Analysis

Our strategy to answer the primary question was to separate both groups of biotechnology companies into winning and losing product subgroups. Trial winners were defined as products that successfully demonstrated clinical efficacy on the prespecified disease end point of interest to enable licensing and successful launching of the product to a substantial market. Trial losers were defined as products that did not demonstrate a statistically significant beneficial effect on the prespecified primary endpoint. For the FDA Advisory Panel reviews, advisory panel winners were defined as products that were given a positive recommendation for market approval by the panel. Advisory panel losers were defined as products that were given a negative recommendation for market approval. We then compared the average percent change of stock prices between winners and losers from the start of the sample period (day −120) to 3 days before critical public announcement events (day −3). Three days before the announcement date was chosen for both groups to avoid sampling any spurious market perturbations due to increased speculative activity, which can occur in the days just before the public unveiling of price-influencing information. For sensitivity analysis, we also compared the average between winners and losers for both groups from day −120 to day −2, and day −120 and day −1. A t test was used for statistical comparison of group averages, with an α value of 0.05 selected for statistical significance.

RESULTS

Group 1: Phase III Clinical Trial Results

A total of 98 biotechnology products that underwent Phase III clinical trials for FDA approval were included in this study. Of the 98 products, 50 were labeled trial winners on the basis of their successful clinical trial outcomes. Figure 1 shows the average price increase for trial winners from day −120 to day +120, a total of 12 calendar months. Day 0, the date of announcement of Phase III results, is represented by a vertical line through the center of the graph. Prices are expressed in percent change from the first day of recording. The price increase over the entire recorded trading period was +76%. The concurrently recorded NASDAQ index average, shown in Figure 1, increased +27% over the same period.

The remaining 48 products in group 1 had a negative outcome at Phase III clinical trials. The average percent change in stock prices for companies attempting to launch these products is shown in Figure 2. Average price trended downward for a total loss of −43% for the entire trading

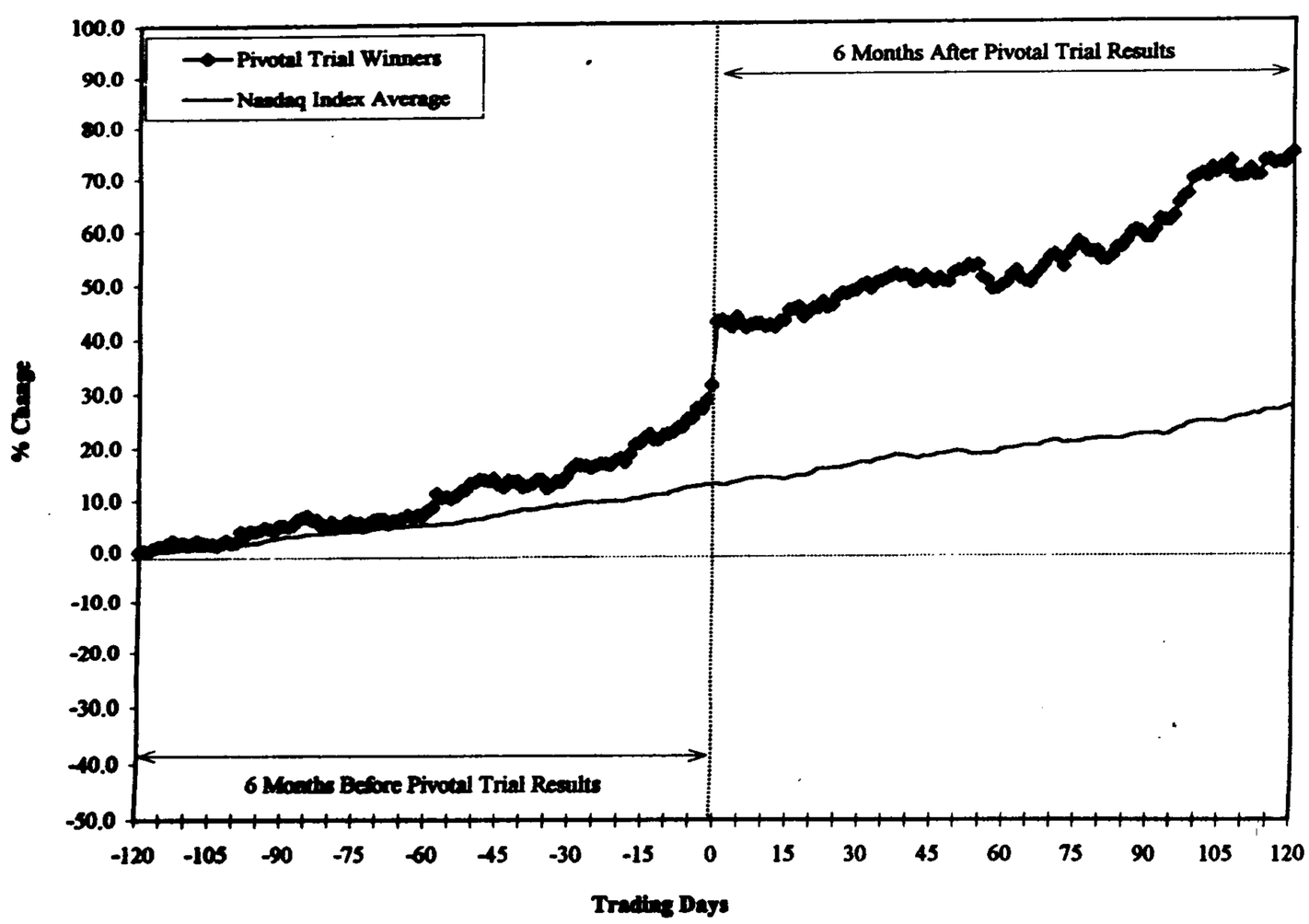

Figure 1. *Average percent change of biotechnology company stock prices for Phase III clinical trial winning products (n=50). The y-axis refers to average percent change of sample stock prices, and the x-axis refers to the number of trading days that prices were recorded (120 trading days=6 calendar months). The vertical line at day 0 refers to the date of public announcement of trial results. The simultaneously recorded NASDAQ system index average is displayed for a concurrent market reference.*

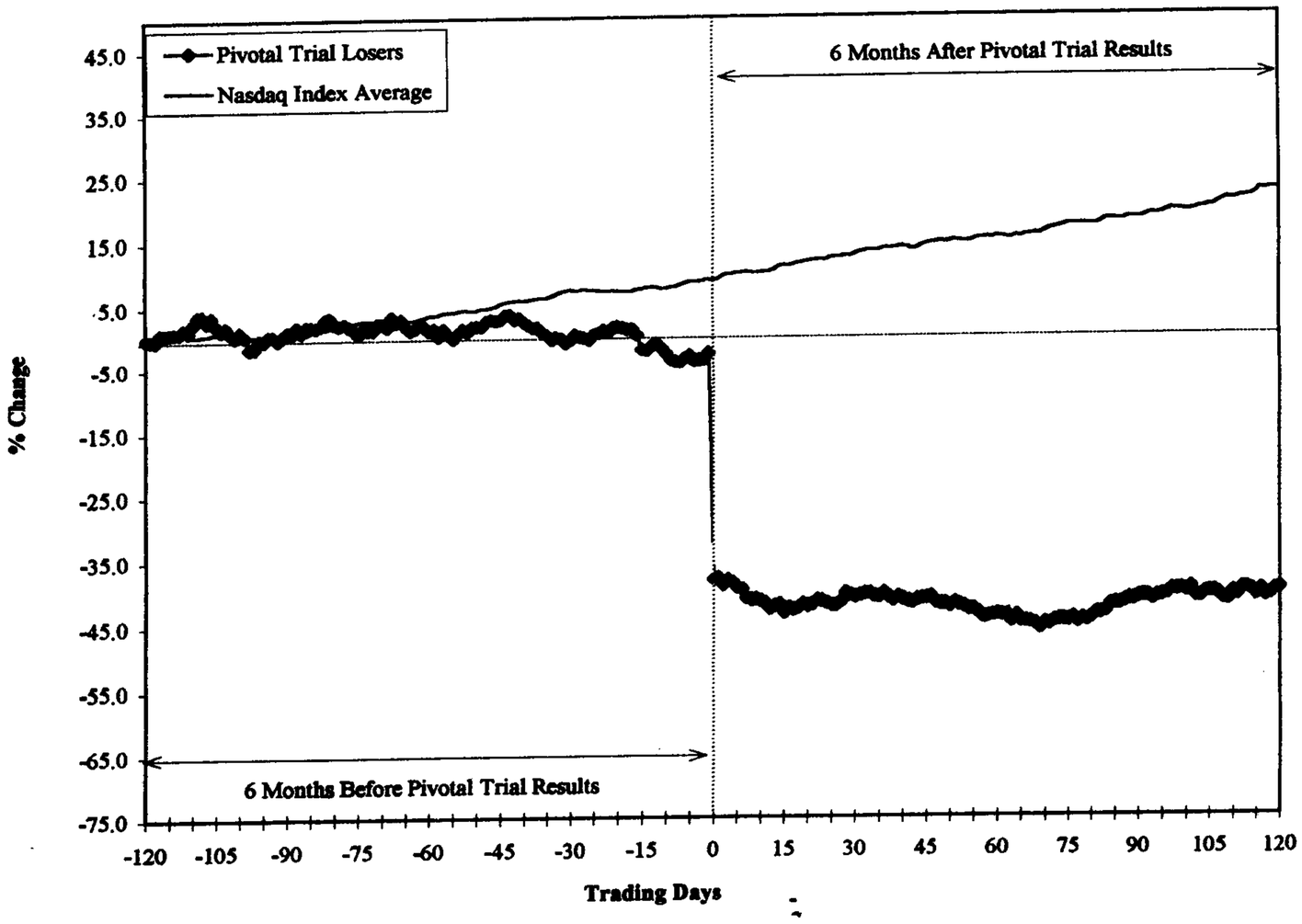

Figure 2. Average percent change of biotechnology company stock prices for Phase III clinical trial losing products (n=48).

period. The simultaneously recorded NASDAQ index average trended up to end at +20% at the end of the study period.

Group 2: FDA Advisory Panel Review Results

Forty-nine biotechnology products undergoing FDA Advisory Panel review were included in this study. Of these, the average percent price change for 36 Advisory Panel winners is shown in Figure 3. The average price of their company's stocks increased to +47% at the end of the recorded study period (day +120). The simultaneous NASDAQ index average increased by +22% over the same time period.

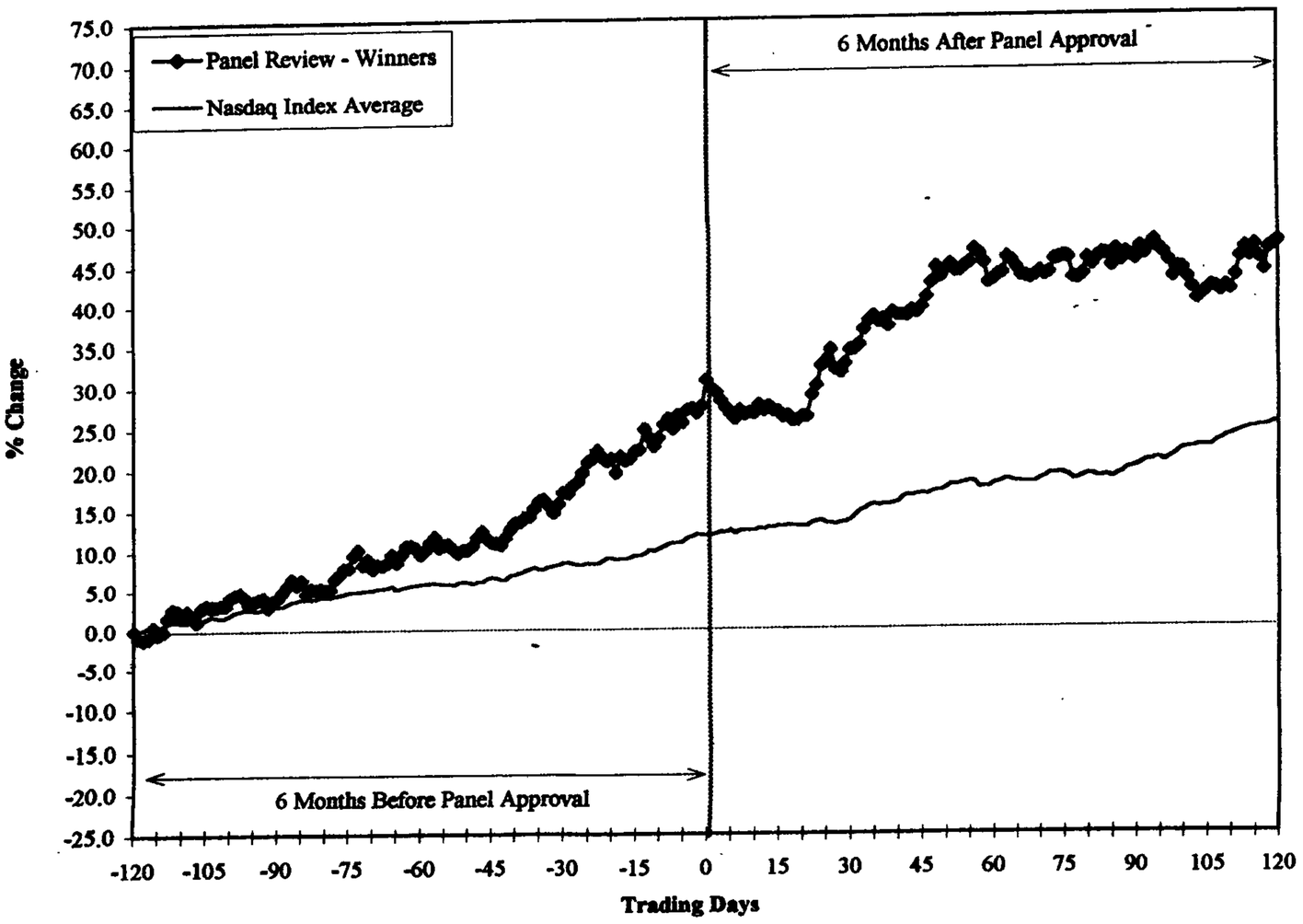

Figure 3. Average percent change of FDA Advisory Panel review results for winning products (n=36).

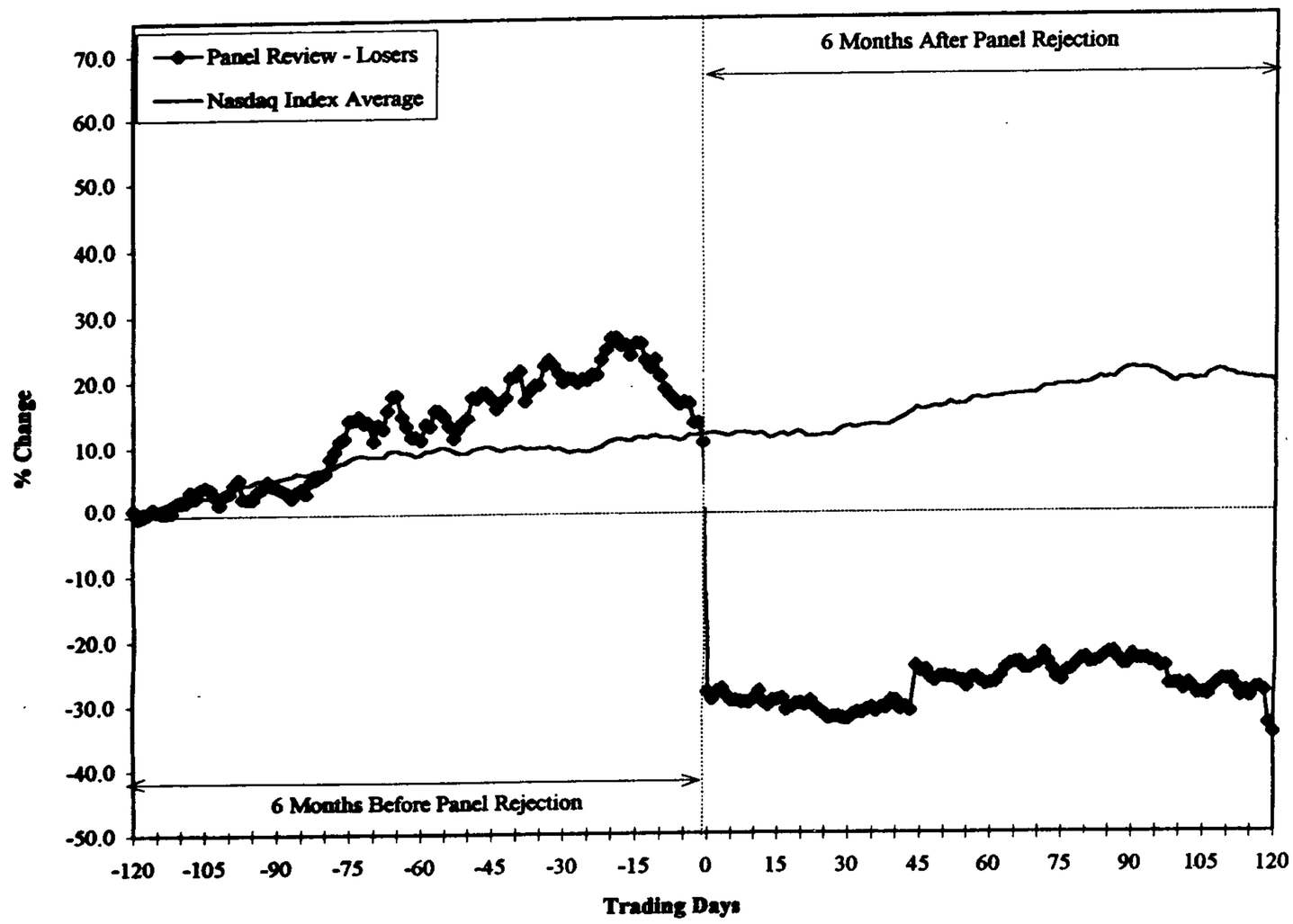

Figure 4. *Average percent change of FDA Advisory Panel review results for losing products (n=13).*

Figure 4 shows the average percent price change for the 13 Advisory Panel losers over the 12 calendar month study period. The average percent price dropped to −37% by day +120. The simultaneous NASDAQ index average increased throughout the study period to +20% on the last recorded date in the study.

Statistical Comparison

Average percent change in stock prices for Group 1 were compared between companies with winning products (n=50) and those with losing products (n=48). This was done by comparing the average price change of each group from day −120 to day −3 before the date of announcement of Phase III clinical trial results (Table 1). The average gain in price for winning trials was +27% just before trial outcome announcement. Average loss for trial losers was −4%. A *t* test statistical comparison showed that there was a highly significant statistical difference in average price between trial winners versus trial losers 3 days before the date of announcement (P=0.0007). The 95% confidence interval for the difference between trial winners and trial losers was +13% to +48% (Tables 1 and 2)

Table 1 also displays the average stock price changes from day −120 to day −3 for FDA Advisory Panel winners (n=36) and losers (n=13). The average gain in panel review winners was +27% on day −3 before the announcements. Trial losers averaged a gain of +13% in the same recorded time frame. A Welch modified *t* test was used for statistical analysis for this study population because of the large price variation in the winning subpopulation. The average price differences were not statistically significant between the winners and losers (P=0.25), although the 95% confidence interval for the difference between the FDA advisory panel winners and losers showed a trend in favor of a difference (−10% to +38%).

A sensitivity analysis was performed for the average change between winners and losers from day −120 to day −2, and day −120 to day −1 (Table 2). This was done to examine whether there were any significant differences in the data during potential speculative market perturbations close to the date of announcement of clinical trial outcomes. The results were similar to our initial day −120 to day −3 analysis and trend toward an increased difference

Table 1. Primary analysis: Average percent change of stock price from day −120 to day −3, before public announcement of product outcomes.

	Winners (% Δ)	Losers (% Δ)	*P*
Group 1–Pivotal trials (n=98)	27 (52)	−4 (33)	0.0007
Group 2–FDA Advisory Panel reviews (n=49)	27 (36)	13 (36)	0.25

Values in parentheses indicate SD.

Table 2. Secondary analysis: Average percent change of stock price before public announcement of product outcomes from day −120 to day −2, and day −120 to day −1.

	Winners (% Δ)	Losers (% Δ)	*P*
Price change from day −120 to day −2			
Group 1–Pivotal trials (n=98)	29 (54)	−4 (33)	0.0005
Group 2–FDA Advisory Panel reviews (n=49)	27 (35)	13 (37)	0.25
Price change from day −120 to day −1			
Group 1–Pivotal trials (n=98)	31 (55)	−3 (34)	0.0004
Group 2–FDA Advisory Panel reviews (n=49)	27 (35)	10 (37)	0.14

Values in parentheses indicate SD.

between winning and losing groups for both Phase III trial results and FDA Advisory Panel review results (Table 2).

DISCUSSION

In this study we found that in biotechnology products undergoing Phase III clinical trials, there was a significant difference in average stock price between trial winners and trial losers in the time period before the public announcement of results. In products undergoing FDA Advisory Panel review, there was a difference between the average price of successful versus unsuccessful biotechnology products that was not statistically significant.

All data were obtained through retrospective examination of daily stock prices at market close of 70 well established biotechnology companies. An advantage of using this method to explore this issue is that it provided us with objective data that were easy to interpret. However, no attempt was made to provide any direct evidence that insider trading is occurring. Therefore, although this phenomenon could explain the observed trends, other important possibilities exist.

Given the highly sensitive nature of biotechnology stock prices as products approach maturity, these markets may react more dramatically to accurate forecasting of a product's outcome. One could make the theoretical argument that it might only require a small number of investors who correctly predict the future success of a highly anticipated product to start a market trend in a consistent direction. However, it is exceedingly unlikely that the small number of investors who begin the price momentum could consistently make correct guesses. Also, although speculative investment activity clearly increases as product announcements are imminent, this is more likely to be reflected in an increase in trading volume, rather than in price change.

An argument could also be made for accurate prediction based on a product's prior track record.[2] Careful investigation can reveal if a potential therapeutic had previously been the subject of well-designed animal studies and Phase II clinical trials, with highly significant and/or convincing results. Thus, expert analysts and other knowledgeable forecasters might theoretically be able to rely on past scientific data to make accurate investment choices. Historically, however, evidence from Phase II trials frequently fails to predict future results. Additionally, as these data have been available for review even before the initiation of Phase III trials, it would not explain the difference just before Phase III data release. This argument implies that interest in existing data on a product consistently increases in the few months before announcement of trial results, leading to differential trends in stock prices.

Analysis of stock prices before the FDA Advisory Panel review announcements revealed a nonsignificant difference between winning and losing products. It may be that at this late stage in a product's development, there may be less speculative interest, because information regarding its efficacy has already been widely publicized in the scientific and financial communities.

Scientific Research and Insider Trading

It has been known for some time that the lengthy scientific process of clinical trials followed by publication of data after peer review may provide opportunities for insider trading to occur.[4,5,7–15] An understanding of biotechnology product development through the FDA process allows speculation as to who could be involved. Months before public announcement of product trial results, it is possible to envision that principal investigators themselves, as well as employees of companies sponsoring the research may be privy to nonpublic, price-influencing information.[5] As the product moves closer to the date of announcement, the circle of individuals who are aware of confidential results might include data management companies, trial manuscript writing committees, scientific reviewers, outside consultants, and scientific journal staff. Finally, reporters and investigative clients may become cognizant of the specific details of the material information before the general public is made aware. Financial analysts could become privy to this information through connections at any stage along the way, acting as a conduit for further dissemination of information. Any obvious price trend started by knowledgeable insiders could then become amplified on the market.

Many potential reasons exist for why an individual might trade on or dispense nonpublic information. Perhaps the most obvious one is that for individuals working closely with price-influencing data, the temptation to reap

personal financial reward may simply be too great. A recent example was the lawsuit filed by the Securities and Exchange Commission (SEC) against Dale J. Lange, a neurologist who was participating in a clinical trial of the drug Myotropin, developed by Cephalon.[16] This clinical investigator agreed to keep confidential any research information he was privy to while testing the product. When he learned of the favorable trial results 1 month before public announcement, he allegedly bought 3000 shares of Cephalon stock, and disseminated the information to six other individuals who followed suit. All of the individuals involved are now being sued by the SEC on the grounds of insider trading.[16]

Another example would be the temptation experienced by an individual who has direct or indirect financial stake in a product known to be a failure. In 1997, the SEC brought a landmark case against Dr. Milton Mutchnik, a gastroenterologist from Wayne State University who was the lead clinical investigator in Phase III Clinical Trials of an anti-hepatitis drug named Thymosin, developed by Alpha I Pharmaceuticals.[11,16] Upon discovery that the drug was not more effective than placebo as an anti-hepatitis agent, he allegedly warned his sister, her husband, and several friends about the results before the public announcement was made. As a result, each informed individual immediately sold their shares of Alpha I stock, thus collectively avoiding approximately $150,000 worth of losses. Dr. Mutchnik was sued by the SEC and eventually settled out of court. This widely publicized case has since been commonly cited as an example of abuse of inside information by a clinical investigator.[11,16]

Another important factor influencing early dissemination of information is the pressure exerted on investigators and others working closely with a product's development. Investors with significant financial stake in a product's performance may in fact pressure investigators to learn confidential information before it becomes public information.[7] Finally, many researchers and people working primarily or exclusively in the scientific field may simply be naïve as to the rules governing their conduct under these circumstances. People who do not work in the business world may be oblivious to the true nature and seriousness of the crime, as was claimed by the investigator from Wayne State.[11]

The rules that the SEC has enforced for years in the business world may only now have begun to be heeded by members of the scientific community involved in price-influencing work. In general terms, insiders who have a fiduciary relationship with the company are barred from trading on nonpublic information, including temporary insiders (eg, lawyers and accountants), as well as outside traders (eg, "tippees").[5,17] Clearly, members of the scientific community at large need to be better educated as to the nature of this obligation when they are involved in material research.

Finally, if those who are involved in research or data management have any potential financial link to the company for whom they are performing the research, full disclosure of these connections should be made.[18] Furthermore, we raise the issue as to whether or not researchers should have equity positions or other types of investment in biomedical or health-related companies rather than other types of business. What may be implied from such 'scientific investment' is that they are attempting to profit from the specialized wisdom that they obtain in the process of performing research.[12]

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