BUSINESS AND REGULATORY NEWS

British Biotech fails to redeem itself

British Biotech (Oxford, UK) has not convinced private and institutional investors that its recent troubles are behind it. On May 19, the company issued a 31-page circular to its shareholders to counter the accusations of its former head of clinical research, Andrew Millar, that company executives had misled investors about the clinical prospects of its pancreatitis drug, Zacutex. On the same day, the company announced at the British Biotech annual general meeting in September that its CEO, Keith McCullagh, would resign—without accepting responsibility for recent events.

Some investors are calling for the resignation of other board members, including the chair, John Raisman. The London Stock Exchange (LSE: London, UK) is conducting an investigation into allegations that the company broke LSE insider-dealing and disclosure rules. "It's John Raisman's job. . .to act in the shareholders' interest," says one investor who would like Raisman to go before the LSE completes its investigation. "He has failed to exercise that responsibility." Others suggest that such a move would only be necessary if the LSE investigation finds against the company. Bob Yerbury, chief investment officer at Perpetual (Henley, UK), which has a 9.44% stake in the firm, says that an adverse LSE outcome would "have implications for management credibility."

Continuing investor concern centers around suggestions that British Biotech is continuing to withhold price-sensitive information about Zacutex's progress from shareholders. Zacutex has been involved in two phase III trials; trial 214 in the United States has been completed and trial 215 in Europe still continues. Much of the data from the second trial was unblinded prematurely and examined by Millar because he thought the trial was not showing efficacy. This led to his well-publicized accusations that British Biotech executives were misleading investors.

Keith McCullagh says that only the computer operators (and Millar, presumably) have the codes to unblind the trials and that there is no data available to send to the markets. The company has taken legal action to recover the data from the trials and associated internal memoranda and notes from Millar. Speaking on June 6, McCullagh told *Nature Biotechnology*, "We do not have access to that data." However, Millar told *Nature Biotechnology* that he had returned all the trial documents to the company on Friday, May 29, after receiving legal threats from the company. When asked about this, McCullagh said that he would have to check whether anything had been received by the company's lawyers. "For the record," he added, "no one at the company has the data."

If the data have been delivered to the company, McCullagh says that British Biotech's next move would have to be to discuss with the European Medicine Evaluation Agency (London) and the US Food and Drug Administration (Rockville, MD) what they should do next. "At the moment [the regulators] are saying don't [publish the unblinded data] and continue the study to its conclusion because so far. . .nobody involved with the study has seen this data and therefore they're not biased."

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McCullagh maintains, therefore, that the company should not preempt the result of the trials. Only 1250 out of 1500 patients have been treated in the European trial, he argues. The trial has been designed to give an 80% chance of showing a 40% reduction in symptoms based on the preliminary results of the earlier and smaller US trial 214. From the trial 214, the company "already has results from three double-blind trials [of Zacutex] which show efficacy." He says, "200 out of 290 patients treated within 48 hours had improved symptoms. And with patients treated within 12 hours, 72% had reduced symptoms." The large European trial 215 was designed to confirm the US study.

Even though, as far as British Biotech is concerned, the results have not been published, a number of people have commented on them. According to reliable sources close to British Biotech, the unblinded data look "scattered and statistically insignificant." Some current senior research and development staff at the company now think there is a less than 1% chance that the drug will succeed. Reliable reports suggest that current senior researchers involved with the running and analysis of the company's clinical research program plan to leave British Biotech if members of the company's board do not resign. If those clinical staff go, all British Biotech's development programs—not just the Zacutex program—could be affected, investors fear.

These unofficial rumblings within the company are making certain investors nervous. They complain that the company has "no intentions to stop these expensive Zacutex trials, despite board-level knowledge that the drug doesn't work." By continuing the trial and refusing to publish the unblinded data, "the company is still misleading the stock market," another investor maintains.

Some analysts, too, are concerned. Nick Woolf of BA Robertson Stephens (London) believes that data from the unblinded trial "should be sent to the market" if it is available. Woolf downgraded the stock from "buy" to "long-term attractive" as soon as he knew that the Zacutex phase III trials may have been compromised in the eyes of the regulators because of the unauthorized unblindings. Woolf would also like to see McCullagh resign before the British Biotech AGM: "If they instill some new blood, rather than promoting people within the company, that would help restore investor confidence."

However, Bob Yerbury of Perpetual has found some reassurance in the detailed discussions he had with British Biotech at the beginning of June. The company will focus primarily on developing its matrix metalloproteinase inhibitors, especially marimastat for metastatic cancer. The remaining concern is that British Biotech's current cash burn rate—£50 million a year—would exhaust the company's coffers before marimastat reached the market in 2002. British Biotech did announce 14% reduction in staff in its May 19 circular, but it needs to reduce its expenses at least 25%. In that context, the continuing cost of the Zacutex trials looks like a significant burden.

An HSBC Securities (London) valuation report on British Biotech appeared on May 20, just after the most recent British Biotech announcements. It valued the company's shares at £0.34, around 40% less than its actual price on that day, with around £0.20 of that valuation coming from British Biotech's £132 million in cash. HSBC attributes no value to Zacutex in Europe. A spokesperson for HSBC says that an adverse outcome from the LSE investigation would "clearly be a future downside for the share price." He does not see investor confidence returning until "the regulatory issues are cleared up and the technology is shown to be good."

Adam Michael