

▶ **Victory for Vitrase?**

Clinical trials of this prospective drug for retinopathy created a roller-coaster effect on the maker's stock price.

BY MARK S. LESNEY

Now that Wall Street traders pay as much attention to clinical results as do research scientists (though for vastly different reasons), the promise or failure of a clinical trial can have a skyrocketing or devastating effect on corporate stock prices. The Imclone scandal involving Martha Stewart is but one high-profile example. Yet it is not insider trading that most affects corporate stability. According to a May 2002 report



Retinopathy's effect on vision is shown at right.

by the Trout Group LLC, "In addition to politics and accounting, this sector [biotech] has the everlasting specter of the FDA and failed clinical trials to blame" (1).

This past January, for example, ISTA Pharmaceuticals (Irvine, CA) promised release of Phase III clinical trial analysis for its new drug Vitrase. A formulation of the enzyme hyaluronidase, Vitrase was being tested for its effects on diabetic retinopathy—one of the most prevalent causes of blindness, affecting some 450,000 people in the United States alone. Diabetic retinopathy is a disease of the blood vessels in the retina. Proliferation of vessels in the retina and spontaneous bleeding can lead to vitreous hemor-

rhage-induced cloudiness and edema.

ISTA was proceeding with Vitrase on an FDA fast track, prompted by the fact that there are no significant nonsurgical treatments for retinopathy and new drugs are badly needed. Fast-track designation allows for submission of components of the NDA (New Drug Application) statement in advance. But the clinical trial did not go according to plan. When ISTA finally announced in March that Vitrase, contrary to hopes, produced no statistically significant clearing of the vitreous humor, its stock took an immediate tumble, from \$2.88 to \$0.91 (2).

However, that was not the end of the story. Despite having the originally chosen end point for the trial fall through, ISTA researchers noticed that Vitrase performed well on a secondary end point—improvement of patient "best-corrected visual acuity". ISTA approached the FDA and received permission to proceed with its NDA based upon the new end point and moved forward with the approval process. Upon release of this information regarding the now-acceptable nature of the trial results in April, stock prices jumped from \$0.83 to \$1.27. In July, ISTA announced it was entering into partnership with Cardinal Health Sterile Technologies to manufacture the intravitreous-injected drug, once final FDA approval is received, as the company hopes it will be, on the manufacturing and controls sections of the NDA, which were submitted at the end of the third quarter of 2002, and the final component of manufacturing validation, which is planned to be submitted in the first quarter of 2003 (3).

If current projections are correct and Vitrase receives approval and becomes available in 2003, it will be a success story from a potential failure. But for all the hopes of having a new drug to combat blindness,

the key lesson of the Vitrase story may be the tight link between clinical trials and financial profits. For good or ill, clinical trials have become an important bellwether for stock market analysts to use in evaluating the health of pharmaceutical biotech companies. And ISTA is not alone, as a host of other companies rode the roller coaster of clinical good news/bad news in 2002 (2).

Less stable and less lucky ventures than ISTA might have failed on the initial stock collapse, with the potential benefits of the drug lost, or at least greatly postponed. And how will other drugs in the pipeline fare when the failure of leading test products can cause such a market fall? When innovation rides the thin line of financial chaos, bad things can happen to good companies. There are no easy answers, and for the foreseeable future the general health of the biotech sector, as well as the patients for whom drugs are being developed, will remain tightly bound to the results and the rumors of clinical trials.

References

- (1) The Trout Group. Instability in the Biotech Sector; May 13, 2002; www.troutgroup.com/Documents/Instability_051302.pdf.
- (2) Biotech flails in 2002 while investors "Wait it Out"; http://bioforest.biospace.com/news_story.cfm?story10=90690198&full=1.
- (3) ISTA Pharmaceuticals, Inc.; www.istavision.com. ■

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www.clinicaltrials.gov

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