

DRUG DEVELOPMENT COURSE 2006

GROUP PROJECT #4.

You are employed by a small biotechnology company that has just finished developing and evaluating an exciting new treatment for Alzheimer's disease. This is a small molecule that interferes with the polymerization of the amyloid-like fibrils seen in the brains of Alzheimer's victims, and it is the only product your company owns that is likely to be approved and marketed in the next 5-6 years. The drug is orally administered, and after Phase II studies a single oral dose of 100 mg B.I.D. was selected for evaluation in a large double-blind randomized placebo-controlled clinical trial in 3000 patients with newly diagnosed Alzheimer's disease.

The Phase III study has now been completed and the blind has been broken. After a median treatment duration of 18 months, the treatment arm receiving your drug, amylex, had their rate of progression of neurocognitive deficits reduced by 50% on average as compared to patients assigned to the placebo arm, a highly statistically significant result ($p < .000000000001$). However, in reviewing toxicities, it was noted that among the 1500 patients taking amylex, there were two cases of fatal hepatic necrosis which investigators labeled as "possibly related to study drug." No cases of hepatic necrosis occurred in the placebo arm, and there were no other differences in toxicity between the two arms.

ADDRESS THE FOLLOWING QUESTIONS:

1. What will you propose be done about these possible fatal drug toxicities?
2. Will you proceed with submission of an NDA for this drug and ask for FDA approval, as your Board of Directors expects?
3. If you proceed with an NDA filing, how will you handle the two cases of fatal hepatic necrosis in hearings before the FDA Advisory Panel and in your proposed package insert for this drug?