Email: vcox@oc.fda.gov

Re: IND 7517 for CN706 and IND 8392 for CV787

Ladies and Gentleman:

Good evening. My name is Dan Henderson, and I am President of Calydon. Calydon is located locally in Sunnyvale, CA and is involved in cancer therapy using adenovirus. Indeed, we use targeted replicating adenovirus to treat prostate cancer. We are currently in the clinic with CN706 and CV787 for the treatment of locally recurrent prostate cancer. More significantly earlier this month we received RAC clearance to treat end-stage metastatic hormone refractory prostate cancer with the intravenous administration of CV787. Clearly, we are a stakeholder in the field.

After the tragic and unfortunate death of Jesse Gelsinger in Philadelphia last September, the adenovirus gene therapy field has been going through a significant re-evaluation. Some of this re-evaluation has centered on the fundamental disconnect prevalent in the field of using a vector that gives transient gene expression but limited usage due to its immunogenicity, to treat genetic defects that require life-long gene expression. Some of the re-evaluation has been to challenge the relationships between clinical investigators, their commitment to the therapy in question, and their financial interests. Equally important has been the need to assure the compliance of unsophisticated sponsors and clinical investigators with the rigorous manufacturing and reporting requirements of all clinical trials. I applaud and wish to express my support of all these efforts.

In addition, I want to express my appreciation of the FDA. Since my first interaction with Phil Nagouchi five years ago to my most recent interaction with Ann Pilaro last week, I have found the FDA professional, supportive, and extremely helpful. I wish to express my thanks.

There is one point I need to make. This relates to the serious adverse event or SAE perpetrated on the whole gene therapy field, and the adenovirus field in particular, for the reckless misadventures of a small minority. To quantify this let me describe the effect on patient enrollment we have experienced at Calydon. In our multi-center clinical trials with adenovirus treating prostate cancer, we have only treated two men with CV787 since mid-October. As recently as last November we projected to have treated 54 men with CV787 by the end of March 2000. However, the inability of local IRBs to distinguish the safety of adenovirus, or the appropriateness of the therapeutic in question for the disease in question, not a single new clinical trial site has come online and treated a patient. This has cost prostate cancer patients dearly; for them a promising new therapy have been needlessly delayed.

The greatest misadventures have occurred at NIH funded sites, by NIH funded investigators, who have recently started companies. Much ado has been made of the commercial interests now seen in the field. However, the misadventures have come from unsophisticated new participants in the world of business. Like youngsters in a candy store, or travelers in a foreign country, mischief can occur when one does not know the limits of participating in new environments. With the proposals of the past few weeks, NIH investigators will start to come up to the necessary FDA imposed levels of clinical conduct, a level of conduct that has been known to most of private industry for decades.

In the case of adenovirus based therapies, the commercial interests, including Calydon, have treated a great number of patients with cancer without mishap. Going forward I urge the FDA to help differentiate the participants in the field, so that the miscreants can be more readily isolated from the whole; to use a cancer example, to separate the tumor tissue from the normal tissue. Negative comments, in the absence of differentiation, brings everyone down to the same level. Perhaps some balancing positive comments would be appropriate.

Thank you.

D.R. Henderson

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