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Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Attn: Robert Justice, MD, HFD-150
Division Director, Division of Oncology Drug Products

Re: CDRH PreIDE #I090606
Phase II Prospective Study Evaluating the Role of Pemetrexed Plus Gemcitabine Chemotherapy for Chemo-naïve Select Stage IIIB and IV Non-Small Cell Lung Cancer (NSCLC) in Patients Using a Genome Predictor of Platinum-Resistance to Guide Therapy

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Dear Dr. Justice:

We received the Agency's assessment of the regulatory oversight required of the above referenced clinical study, and we would like to ask for clarification regarding the conclusion that the study design presents a significant risk to the subjects. Our team has performed a number of clinical studies using approved drugs off-label and we take very seriously the importance of ensuring subject safety. However, given the acceptance by the oncology profession for this particular drug combination in treating NSCLC, we were surprised by the Agency's conclusion that this study presented a significant risk to the patients. The primary reason that we are requesting this additional clarification is to better understand the Agency's reasoning as we are planning to conduct additional genomic-guided clinical studies in the future and this will help us in our planning.

The Agency's assessment of significant risk focused on two issues; the potential assignment of a chemo-naïve NSCLC patient to a non-platinum based chemotherapy treatment and that patients with predominant squamous NSCLC should not receive pemetrexed. Regarding the issue of squamous NSCLC, the protocol has been revised wherein patients with this type of cancer will not be assigned to pemetrexed therapy (Please see attached study protocol).

While it is acknowledged that platinum-based therapy is considered first line therapy for NSCLC, non-platinum based therapy is also considered acceptable first line therapy per current ASCO and NCCN guidelines and is infact being used currently in at least 13 phase II/III trials (www.clinicaltrials.gov).

We have attached the revised version of the protocol for any further clarifications. Should the Agency still feel that the study design presents a significant risk to patients after the change to the protocol that is now consistent with the recent ASCO and NCCN guidelines for NSCLC, we will of course quickly submit an IND for this study. However, we would appreciate any additional insight to enable us to better plan future studies that may have similar issues.

Thank you for the help and guidance in this matter. Also, I wish you and yours a great holiday season.

Sincerely,

Anil Potti

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