DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 17 1998

WARNING LETTER

Certified Mail
Return Receipt Requested

Reference: 99-HFD-340-1101

Donald E. Johnson, M.D.
3400 NE 192 Court
Apt 1901
Adventura, Florida 33180

Dear Dr.Johnson:

Between September 14-21, 1998, Ms. Angela K. Rhodes, representing the Food and Drug Administration (FDA), inspected your conduct, as the investigator of record, of a clinical study [protocol #[ ]with the investigational new drug Panretin. The study was entitled "Randomized Phase 3 Vehicle Controlled Trial of ALRT1057 Topical Gel in Patients with AIDS-Related Cutaneous Kaposi's Sarcoma," and sponsored by Ligand Pharmaceuticals, Inc.

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects have been protected.

During the exit interview on September 21, 1998, Ms. Rhodes discussed the inspectional observations with and issued a Form FDA 483 to Norman S. Embee, President of the Coleman Institute. From our evaluation of the inspection report and the documents collected during the inspection, we conclude that you violated federal regulations and good clinical practices governing the conduct of clinical investigations and the protection of human subjects. We emphasize that:

I. **You did not conduct your study in accordance with the approved protocol [ ][21 CFR 312.60 and 21 CFR 312.53(c)(1)(vi)(a)].**

Subjects #461, #464, #468 and #472 were administered systemic chemotherapy (Doxil) that was prohibited by the protocol, and this therapy was not reported to the sponsor in the CRFs for subjects #461, #464, and #468.

You failed to obtain required laboratory samples for subject #469 at week 16 and to assess the lesion size for subject #477 at visit 1.

II. **You failed to prepare and maintain adequate and accurate records of all observations and other data pertinent to the investigation for each subject in the clinical study as required by federal regulations [21 CFR 312.62(b)].**

There are inconsistencies between the source data and the CRFs for the lesion measurement of subject #817 and for the vital signs of subject #469 at week 16.

You failed to maintain a copy of the pathology report for subject #457 confirming the diagnosis of Kaposi's Sarcoma.

III. You failed to report all adverse events to the sponsor as required by federal regulations [21 CFR 312.64 (b)].

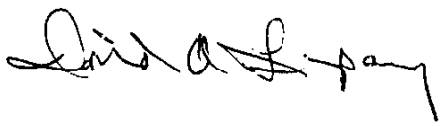
Adverse events for subject #458 were not reported, for example diarrhea and nausea at week 4 and chewing pain at week 8.

The above-mentioned deficiencies are not all inclusive. We have received and reviewed the October 1, 1998 written response of Mr. Embree (Coleman Institute) to Ms. Rhodes that offered his explanations for the items listed on the Form FDA 483.

As summarized above, the FDA inspection documented that you have violated federal regulations governing the clinical study of investigational new drugs. Within 15 calendar days of receipt of this letter, notify this office in writing of the corrective actions you have taken to prevent similar violations in your current and future clinical new drug studies. Your failure to adequately and promptly correct these matters may result in regulatory action without further notice.

Please address your written response and any pertinent documentation to me.

Sincerely yours,



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cc:
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