



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

JUN 30 2008

Robert Cohen, President & CEO
Travanti Pharma, Inc.
2520 Pilot Knob Rd., Suite 100
Mendota Heights, MN 55120

Ref: 08-HFD-45-0601

Dear Mr. Cohen:

Between February 19 and 28, 2008, Ms. Sharon Matson, representing the Food and Drug Administration (FDA), conducted an investigation and met with you to review your firm's practices as the sponsor of the following clinical investigations of the investigational device-drug combination product, [] performed for Travanti Pharma, Inc.:

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]

This inspection is a part of the FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of those studies have been protected.

We are aware that at the conclusion of the inspection, Ms. Matson presented and discussed with you Form FDA 483, Inspectional Observations. From our review of the establishment inspection report, the documents submitted with that report, and your firm's March 11, 2008, letter written in response to the Form FDA 483, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations. We wish to emphasize the following:

1. Failure to submit an IND for the conduct of clinical investigations with an investigational new drug that is subject to 21 CFR 312.2(a) [21 CFR 312.20(a) and 312.40(a)].

FDA regulations at 21 CFR Part 312 contain procedures and requirements governing the use of investigational new drugs. 21 CFR 312.3(b) defines a clinical investigation as “any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.”

An investigational new drug may be used in a clinical investigation if the following conditions are met: the sponsor submits an IND for the drug to FDA, the IND is in effect under FDA regulations, and the sponsor complies with all applicable requirements of 21 CFR Parts 50, 56, and 312; and each participating investigator conducts his investigation in compliance with the requirements of 21 CFR Parts 50, 56, and 312. 21 CFR 312.40(a).

The device-drug combination product of [] is not approved for marketing in the U.S.A. Clinical investigations involving the use of the device-drug combination product, [] that are not exempt from 21 CFR Part 312 must meet the general requirements for use of an investigational new drug in a clinical investigation. See 21 CFR 312.2. The three clinical investigations listed above []

[] appear not to be exempt from 21 CFR 312.2(a) requirements and not within the exemptions of 21 CFR 312.2(b), and therefore required an IND. Thus, Travanti Pharma, Inc., initiated clinical investigations using [] prior to submitting, and having in effect, a required IND application.

2. Failure to obtain an investigator statement, Form FDA 1572, before permitting an investigator to participate in an investigation [21 CFR 312.53(c)(1)].

Specifically, Travanti Pharma, Inc., initiated clinical investigations that were not exempt from the requirements of 21 CFR Part 312 and allowed clinical investigators to participate in the investigation prior to obtaining a signed investigator statement containing:

- a. The name and address of the investigator;
- b. The name and code number, if any, of the protocol(s) in the IND identifying the study(ies) to be conducted by the investigator;

- c. The name and address of any medical school, hospital, or other research facility where the clinical investigation(s) will be conducted;
 - d. The name and address of any clinical laboratory facilities to be used in the study;
 - e. The name and address of the IRB that is responsible for review and approval of the study(ies);
 - f. A commitment by the investigator that he or she:
 - i. Will conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, the rights, or welfare of subjects;
 - ii. Will comply with all requirements regarding the obligations of clinical investigators and all other pertinent requirements in this part;
 - iii. Will personally conduct or supervise the described investigation(s);
 - iv. Will inform any potential subjects that the drugs are being used for investigational purposes and will ensure that the requirements relating to obtaining informed consent (21 CFR part 50) and institutional review board review and approval (21 CFR part 56) are met;
 - v. Will report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 312.64;
 - vi. Has read and understands the information in the investigator's brochure, including the potential risks and side effects of the drug; and
 - vii. Will ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.
 - g. A commitment by the investigator that, for an investigation subject to an institutional review requirement under part 56, an IRB that complies with the requirements of that part will be responsible for the initial and continuing review and approval of the clinical investigation and that the investigator will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others, and will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to the human subjects.
 - h. A list of the names of the sub-investigators (e.g., research fellows, residents) who will be assisting the investigator in the conduct of the investigation(s).
3. Failure to select a monitor qualified by training and experience to monitor the progress of the investigation [21 CFR 312.53(d)].

The FDA inspection disclosed that your firm did not maintain any documentation to indicate that the above studies requiring an IND were adequately monitored.

4. Failure to maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug [CFR 312.57(a)].

The FDA inspection disclosed that your firm did not maintain drug accountability records for the above studies requiring an IND. As a sponsor, your firm is required to maintain drug disposition records to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each such shipment.

5. Failure to maintain complete and accurate records showing any financial interests of investigators under 21 CFR Part 54 as described in 21 CFR 312.57(b).

The FDA inspection disclosed that, for the above studies requiring an IND, your firm did not maintain complete and accurate records showing any financial interest in 21 CFR 54.4(a)(3)(i), (a)(3)(ii), (a)(3)(iii), and (a)(3)(iv) paid to clinical investigators by the sponsor of the covered studies. As a sponsor, your firm is required to maintain complete and accurate records including the following:

- a. Any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of a covered clinical trial, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study [21 CFR 54(a)(3)(i)];
- b. Any significant payments of other sorts from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria [21 CFR 54(a)(3)(ii)];
- c. Any proprietary interest in the tested product held by any clinical investigator involved in a study [21 CFR 54(a)(3)(iii)]; and
- d. Any significant equity interest in the sponsor of the covered study held by any clinical investigator involved in any clinical study [21 CFR 54(a)(3)(i)].

In your firm's March 11, 2008, letter written in response to the Form FDA 483, Inspectional Observations, your firm acknowledged that the clinical investigations with the use of [] should have been conducted under an IND and stated that the other observations were derivatives of not conducting the study under an IND. Your firm's response stated that procedures will be put into place to ensure compliance with the FDA regulations in the future. We acknowledge your firm's assurance that corrective actions will be taken. However, we note that the response did not contain a detailed outline of procedures or processes that would be implemented to prevent the future occurrence of these observations.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of an investigational drug. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You should address these deficiencies and establish procedures to ensure that any on-going or future studies will be in compliance with FDA regulations.

Within fifteen (15) working days of your receipt of this letter, you should notify this office in writing of the actions you have taken or will be taking (including corrective action plans and standard operating procedures) to prevent similar violations in the

future. Failure to adequately and promptly explain the violations noted above may result in regulatory action without further notice.

If you have any questions, please contact Constance Lewin, M.D., M.P.H., at 301-796-3397; FAX 301-847-8747. Your written response and any pertinent documentation should be addressed to:

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Sincerely yours,



Leslie K. Ball, M.D.
Director
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