DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-260/S-006

Ligand Pharmaceuticals, Inc.
10275 Science Center Drive
San Diego, CA 92121-1117

Attention: James L'Italien, PhD
Sr. Vice President, Regulatory Affairs and Compliance

Dear Dr. L'Italien:

Please refer to your supplemental new drug application dated August 8, 2005, received August 9, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for AVINZA® (morphine sulfate extended-release capsules).

We acknowledge receipt of your submissions dated September 13 and September 15, 2005.

This "Changes Being Effected in 30 Days" supplemental new drug application provides for changes to the BOXED WARNING; CLINICAL PHARMACOLOGY section, *In Vitro AVINZA-Alcohol Interaction* subsection; WARNINGS section, *Interactions with Alcohol and Drugs of Abuse* subsection; PRECAUTIONS section, *Information for Patients* subsection; and DOSAGE AND ADMINISTRATION section of the package insert that highlight and strengthen the warning that patients should not consume alcohol while taking AVINZA®.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit an electronic version of the FPL according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format - NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "FPL for approved supplement NDA 21-260/S-006." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Lisa Basham-Cruz, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bob Rappaport

10/18/2005 05:38:40 PM