DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 19818/S-053

SUPPLEMENT APPROVAL

Sigma-Tau Pharmaceuticals, Inc.
Attention: Gianfranco Fornasini, Ph.D.
Senior Vice President, Scientific Affairs
9841 Washingtonian Blvd.
Gaithersburg, MD 20878

Dear Dr. Fornasini:

Please refer to your Supplemental New Drug Application (sNDA) dated December 19, 2013, received December 20, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Adagen® (pegademase bovine) Injection, 250 units/mL.

This Prior Approval supplemental new drug application proposes revisions to the **ADVERSE REACTIONS** and **HOW SUPPLIED** sections of the package insert:

APPROVAL & LABELING

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text which is identical to the labeling text submitted on December 19, 2013.

LABELING REVISIONS

The following revisions have been made in the package insert (added text is underlined, and deleted text is ~~strikethrough~~.)

1. In the **ADVERSE REACTIONS** section, the third paragraph has been revised as follows:

   Hematologic events: hemolytic anemia, auto-immune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia.
   Dermatological events: injection site erythema, urticaria.
   Lymphomas

2. In the **HOW SUPPLIED** section, the first paragraph has been revised as follows:

   ADAGEN® (pegademase bovine) Injection is a clear, colorless, preservative free solution for intramuscular injection. ~~Each vial contains 250 units/mL and~~ **ADAGEN**® is supplied as a sterile solution in single-use vials containing 375 units per 1.5 mL solution single-use vial, in boxes of 4 vials (NDC-57665-001-01).

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

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 Lois Almoza, MS, Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, M.D., M.P.H.
Deputy Director for Safety
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling (Package Insert)

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

/s/

OZLEM A BELEN
06/05/2014