DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125293/S-085

**SUPPLEMENT APPROVAL**
**FULFILLMENT OF POSTMARKETING REQUIREMENT**

Crealta Pharmaceuticals LLC
c/o Horizon Pharma Rheumatology LLC
150 Saunders Road, Suite 400
Lake Forest, IL 60045

Attention: Claudia Caggiano
Associate Director, Regulatory Affairs

Dear Ms. Caggiano:

Please refer to your Supplemental Biologics License Application (sBLA), dated November 10, 2015, received November 10, 2015, and your amendments, submitted under section 351(a) of the Public Health Service Act for Krystexxa (pegloticase) Injection, 8 mg/mL.

This Prior Approval supplemental biologics application proposes updates to section 13.2 of the Package Insert (PI) to include the results of an 18-month nonclinical study. This study was conducted to address the Postmarketing Requirement Study (PMR) 2569-5, listed in the approval letter for BLA 125293/0 dated September 14, 2010. This supplement is in response to the Agency Supplement Request letter dated September 11, 2015.

## APPROVAL & LABELING

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

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, and text for the Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.
The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

## REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

## FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We acknowledge receipt of your submission dated September 11, 2014, containing the final report for the following postmarketing requirement listed in the September 14, 2010, approval letter for BLA 125293.

2569-5 Conduct an 18-month study in dogs to evaluate the impact of cytoplasmic vacuoles in the adrenal gland and the aortic outflow tract of the heart.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there is a postmarketing requirement listed in the September 14, 2010 approval letter that is still open.

## REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Carol F. Hill, Senior Regulatory Health Project Manager for Safety, at (301) 796-1226.

Sincerely,

*{See appended electronic signature page}*

Sally Seymour, MD
Deputy Director for Safety
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

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/s/

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SALLY M SEYMOUR
05/10/2016