DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 208051/S-002

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT AND COMMITMENT

Puma Biotechnology, Inc
Attention: Jesse Ho, Pharm D
Associate Director, Regulatory Affairs
10880 Wilshire Blvd, Suite 2150
Los Angeles, CA 90024-4800

Dear Dr. Ho:

Please refer to your Supplemental New Drug Application (sNDA) dated January 8, 2018, received January 8, 2018, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nerlynx® (neratinib maleate) tablets, 40 mg.

This Prior Approval supplemental new drug application provides for updates to the Nerlynx® USPI based on the final reports submitted for the postmarketing requirement and commitment on the 2-year rat carcinogenicity study and H2-receptor antagonist drug-drug interaction study.

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 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 package insert and text for the patient 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 include 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).

FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENT

With the review of this submission, we have concluded that the following requirement and commitment were fulfilled:

3223-2 To assess carcinogenic potential conduct a 2-year carcinogenicity study in the rat. Refer to the ICH S1A Guidance for Industry on *The Need for Long Term Rodent Carcinogenicity Studies of Pharmaceuticals.*

3223-5 Conduct a clinical pharmacokinetic trial to evaluate whether separating the dosing of H2-receptor antagonists and neratinib can minimize the drug-drug interaction potential. Submit Final Report with Datasets.

We remind you that there are postmarketing requirements and postmarketing commitments listed in the July 17, 2017 approval letter that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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 Fatima Rizvi, Regulatory Project Manager, at (240) 402-7426.

Sincerely,

{See appended electronic signature page}

Laleh Amiri-Kordestani, MD
Acting Supervisory Associate Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

/s/

LALEH AMIRI KORDESTANI
06/28/2018