DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022-393/S-011

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Celgene Corporation
Attention: Suzette A. Dowling
Director of Regulatory Affairs
400 Connell Drive, Suite 7000
Berkeley Heights, NJ 07922

Dear Ms. Dowling:

Please refer to your Supplemental New Drug Application (sNDA) dated December 21, 2012, received December 26, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Istodax® (romidepsin) lyophilized powder.

We acknowledge receipt of your amendments dated April 2, May 1, and May 31, 2013.

This "Prior Approval" supplemental new drug application provides for revised labeling to Section 7. DRUG INTERACTIONS in the Istodax package insert based on data from study ROMI-ADVM-001 entitled "A Phase 1 Open-Label, 2-Period Study to Evaluate the Influence of Multiple Oral Doses of Ketaconazole on the Single Dose Pharmacokinetics of Romidepsin in Subjects with Advanced Cancer" to fulfill PMR 1556-5 and study ROMI-ADVM-002 entitled "A Phase I Open-Label, 2-Period Study to Evaluate the Influence of Multiple Oral Doses of Rifampin on the Single Dose Pharmacokinetics of Romidepsin in Subjects with Advanced Cancer" to fulfill PMR 1556-6.

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 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).

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 have received your submissions dated December 21, 2012 and April 2, 2013 containing the final reports for the following postmarketing requirements listed in the November 5, 2009 approval letter.

PMR 1556-5 Conduct a drug interaction clinical trial with a CYP3A4 inhibitor, ketoconazole, in patients with advanced cancer. This trial will be a crossover design to evaluate the effects of ketoconazole on the pharmacokinetic disposition of romidepsin.

The timetable you submitted on October 14, 2009, states that you will conduct this trial according to the following timetable:

Final Protocol Submission:	July 31, 2010
Trial Completion Date:	July 31, 2012
Final Report Submission:	December 31, 2012

PMR 1556-6 Conduct a drug interaction clinical trial with a CYP3A4 inducer, rifampin, in patients with advanced cancer. This trial will be a crossover design to evaluate the

effects of induction of CYP3A4 by rifampin on the pharmacokinetic disposition of romidepsin.

The timetable you submitted on October 14, 2009, states that you will conduct this trial according to the following timetable:

Final Protocol Submission:	July 21, 2010
Trial Completion Date:	July 31, 2012
Final Report Submission:	December 31, 2012.

We have reviewed your submissions and conclude that the above requirements were fulfilled.

We remind you that there is a postmarketing requirement listed in the November 5, 2009 Approval letter and a postmarketing requirement and a postmarketing commitment listed in the June 16, 2011 approval letter for S-004 that are still open.

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 Patricia Garvey, Regulatory Project Manager, at (301) 796-8493.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, M.D.
Deputy Director for Safety
Division of Hematology
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/

ROBERT C KANE
06/13/2013