

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

***APPLICATION NUMBER:***

**202497Orig1s000**

***Trade Name:*** Marqibo

***Generic Name:*** vinCRISTine sulfate LIPOSOME injection

***Sponsor:*** Talon Therapeutics, Inc.

***Approval Date:***  
August 9, 2012

***Indications:*** For the use of Marqibo (vinCRISTine sulfate LIPOSOME injection) for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies.

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## 202497Orig1s000

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*APPLICATION NUMBER:*

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**APPROVAL LETTER**



NDA 202497

**ACCELERATED APPROVAL**

Talon Therapeutics, Inc.  
Attention: Thomas J. Tarlow  
Vice President, Regulatory Affairs and Quality Assurance  
400 Oyster Point Blvd, Suite 200  
South San Francisco, CA 94080

Dear Mr. Tarlow:

Please refer to your New Drug Application (NDA) dated July 12, 2011, received July 12, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Marqibo (vinCRISTine sulfate LIPOSOME injection).

We acknowledge receipt of your amendments dated September 6 and 20, October 12 and 20, November 8 and December 2, 2011; January 25 and 27, February 13 and 28, March 13, April 10, 12, and 19, May 3, July 12 and 18, 2012.

This new drug application provides for the use of Marqibo (vinCRISTine sulfate LIPOSOME injection) for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies.

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text and required patient labeling. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

## **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, text for the patient package insert). 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.

## **CARTON AND IMMEDIATE CONTAINER LABELS**

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on August 7, 2012, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).” Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 202497.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

## **ACCELERATED APPROVAL REQUIREMENTS**

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. We remind you of your postmarketing requirement specified in your submission dated August 1, 2012. This requirement, along with required completion dates, is listed below.

- 1910-1 To perform and submit the trial, presently under SPA agreement, TTX404 “A Phase 3, Multicenter, Randomized Study to Evaluate the Substitution of Marqibo (Vincristine Sulfate Liposomes Injection, VSLI) Standard Vincristine Sulfate Injection (VSI) in the Induction, Intensification, and Maintenance Phases of Combination Chemotherapy in the Treatment of Subjects > 60 Years Old with Newly Diagnosed Acute Lymphoblastic Leukemia (ALL)” to address your subpart H commitment according to the timelines below. Any amendments to the SPA trial TTX404 must also be submitted to the PMR.

Report of 1/3 enrollment

12/2014

Report of 2/3 enrollment	12/2015
Report of enrollment completion	12/2016
Study/Trial Completion:	8/2017
Final Report Submission:	4/2018

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirement(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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

### **POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitments:

- 1910-2 Due to the complexity of on site preparation of the final drug product, to study and report at six month intervals on the experience of health care practitioners (HCPs) regarding safety or technical problems with preparation of Marqibo in practice settings.

Preliminary protocol submission (survey and report template FDA submission)	10/2012
Final protocol submission (final survey and report template FDA submission)	12/2012
First 6 monthly report	6/2013
Second interim report	12/2013
Third interim report	6/2014
Fourth interim report	12/2014
Fifth interim report	6/2015
Sixth interim report	12/2015
Seventh interim report	6/2016
Eighth interim report	12/2016
Ninth interim report	6/2017
Final Report	12/2017

1910-3 Considering the relative complexity of preparation of Marqibo, to explore methods to simplify preparation of the final drug product, including the possibility of developing a formulation of liposomal encapsulation such that the step of heating of the drug in the pharmacy is eliminated.

Preliminary protocol submission	12/2012
Final protocol submission	6/2013
Study completion	12/2016
Study report submission to FDA	6/2017

### **PROMOTIONAL MATERIALS**

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved package insert (PI)/Medication Guide/patient PI (as applicable).

Send each submission directly to:

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

### **METHODS VALIDATION**

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

### **REPORTING REQUIREMENTS**

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

If you have any questions, call Amy Baird, Regulatory Project Manager, at (301) 796-4969.

Sincerely,

*{See appended electronic signature page}*

Ann T. Farrell, M.D.  
Director  
Division of Hematology Products  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling  
Carton and Container 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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ANN T FARRELL  
08/09/2012