



BLA 12543/0

Kite Pharma, Incorporated  
ATTENTION: Rizwana F. Sproule, Ph.D.  
Vice President, Regulatory Affairs  
2225 Colorado Avenue  
Santa Monica, CA 90404

Dear Dr. Sproule:

Attached is a copy of the memorandum summarizing your September 11, 2017 Late-Cycle teleconference with CBER. This memorandum constitutes the official record of the teleconference. If your understanding of the teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to the appropriate Submission Tracking Number 125643 in future submissions related to the subject product.

If you have any questions, please contact Regulatory Project Manager, Mark L. Davidson at 240-402-8277.

Sincerely,

Raj K. Puri, M.D., Ph.D.  
Director  
Division of Cellular and Gene Therapies  
Office of Tissues and Advanced Therapies  
Center for Biologics Evaluation and Research

### **Late-Cycle Meeting Summary**

**Meeting Date and Time:** September 11, 2017 1:00-2:30pm

**Meeting Location:** Food and Drug Administration  
Center for Biologics Evaluation and Research  
White Oak-Building 71, Room 5244  
10903 New Hampshire Ave.  
Silver Spring, MD 20993-0002

**Application Number:** 125643/0

**Product Name:** axicabtagene ciloleucel

**Proposed Indications:** for the treatment of relapsed/refractory aggressive B-cell non-Hodgkin lymphoma (NHL) who are ineligible for autologous stem cell transplant (ASCT)

**Applicant Name:** Kite Pharma, Inc.

**Meeting Chair:** Michael Havert, PhD  
**Meeting Recorder:** Mark L. Davidson, DRPM

### **FDA ATTENDEES**

Mike Havert, PhD, Biologist, Product Chair, DCGT/OTAT  
Mark Davidson, RPM, DRPM/CBER/OTAT  
Rachael Anatol, PhD, Deputy Director, OTAT  
Kimberly Benton, PhD, Associate Director for Regulatory Management, OTAT  
Larissa Lapteva, MD, Associate Director, CBER/DCEPT/OTAT  
Steven Oh, PhD, Acting Deputy Director, DCGT  
Denise Gavin, PhD, Branch Chief, CBER/OTAT/DCGT/OTAT  
Ilan Irony, MD, Deputy Director, DCEPT  
Bindu George, MD, Branch Chief, DCEPT/CHB/OTAT  
Najat Bouchkouj, MD, Clinical Safety Reviewer, DCEPT/CHB/OTAT  
Yvette Kasamon, MD, Clinical Efficacy Reviewer, CDER/OHOP/DHP/OCE  
Xiaofei Wang, MD, Clinical Pharmacology Reviewer, OMPT/CBER/OBRR  
Xue (Mary) Lin, PhD, Biostatistics Reviewer, CBER/OBE  
Jinhua Lu, PhD, Pharmacology/Toxicology, OTAT/DCEPT/PTBI  
Jakob Reiser, PhD, Biologist, DCGT/OTAT/ GTIB  
Graeme Price, PhD, Microbiologist, DCGT/OTAT/  
Lori Tull, Deputy Director, DRPM/CBER/OTAT  
Nannette Cagungan, MS, Branch 1, Chief, DRPM  
Scott Proestel, MD, Division Director, CBER/OBE/DE  
Adamma C. Mba-Jonas, MD, Medical Epidemiologist, OBE/DE  
Dennis Cato, Consumer Safety Officer, CBER/OCBQ/BIMO

Colonious King, Consumer Safety Officer, OCBQ/BIMO  
John Eltermann Jr, RPh, MS, Director, CBER/OCBQ/DMPQ  
Donald Ertel, CMDR, CMC Facility Reviewer, CBER/OCBQ/DMPQ  
Wei Wang, Microbiologist, OMPT/CBER/OCBQ/DMPQ/BI  
Carolyn Renshaw, Branch Chief, CBER/OCBQ/DMPQ/BI  
Sarah Lee, Consumer Safety Officer, OCBQ/DMPQ/ ARB  
Lisa Stockbridge, Branch Chief, APLB/ OCBQ  
Dana Jones, Consumer Safety Officer, APLB/ OCBQ  
Amy McKee, MD, Supervisory Associate Director, CDER/OND/OHOP  
Elizabeth Everhart, MSN, RN, ACNP, Senior Drug Risk Analyst,  
CDER/OSE/OMEPRM/DRISK  
Neil Vora, OMPT/CDER/OSE/PMS  
Justin Earp, CDER/OTS/OCP/DPM  
Chao Liu, Visiting Associate, CDER/OTS/OCP/DPM

### **APPLICANT ATTENDEES**

David Chang, MD, PhD Chief Medical Officer and EVP R&D  
Jeff Wiezorek, MD Sr. VP Clinical Development  
William Go, MD, PhD VP Clinical Development  
David Chonzi, MD, VP Safety  
Lynn Navale, VP Biometrics  
Tim Moore, EVP Technical Operations  
Marc Better, PhD, VP Product Sciences  
Kanti Thirumoorthy, PhD, Sr. Dir Quality  
Rizwana Sproule, PhD, VP Regulatory Affairs  
Mehrshid Alai-Safar, PhD, Sr Dir Regulatory CMC  
Alex Babayan, PhD, Ass Dir Regulatory Affairs  
Nadia Agopyan, PhD., Dir Regulatory Affairs

### **BACKGROUND**

BLA 125643/0 was submitted on March 31, 2017 for axicabtagene ciloleucel.

Proposed indication(s): treatment of relapsed/refractory aggressive B-cell non-Hodgkin lymphoma (NHL) who are ineligible for autologous stem cell transplant (ASCT)

PDUFA goal date: November 29, 2017

In preparation for this meeting, FDA issued the Late-cycle Meeting Materials on August 30, 2017.

### **DISCUSSION**

#### **1. Discipline Review Letters**

No Discipline Review letters have been issued to date.

2. Substantive Review Issues to be discussed during the LCM

The following substantive review issues have been identified to date:

**Clinical Efficacy:**

The revised indication under review is for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.

There are insufficient data (two patients) to support an indication (b) (4), and ineligibility for autologous stem cell transplantation was not the entry criterion for the ZUMA1 efficacy population.

**Additional Discussion:**

**Clinical Safety:**

Review of safety data and the 120 Day safety update data are ongoing. We will communicate with you if we have additional information requests or if we identify additional safety concerns.

**CMC:**

As discussed during the July 14, 2017 Mid-cycle Meeting, we have identified issues regarding proposed shelf life for the vector and final product.

The BLA original submission contained stability data which did not support the proposed shelf life for the (b) (4) vector and axicabtagene ciloleucel final product.

Updated stability data provided in amendment 46 (dated August 4, 2017) supports a (b) (4) shelf life for (b) (4) vector stored at (b) (4) and a 12 month shelf life for axicabtagene ciloleucel stored at  $\leq -150^{\circ}\text{C}$ . We recommend that any additional stability data be submitted before September 12, 2017. We recommend that any additional stability data be submitted before September 12, 2017.

**Additional Discussion:**

Updated stability data were provided in amendment 60 (dated 9/11/17) to support an (b) (4) shelf life for (b) (4) vector stored at (b) (4). This amendment is under review.

For inspections: PLI inspections are complete. A final recommendation is pending at this time.

**Advisory Committee Meeting**

An Advisory Committee meeting is not planned.

**Risk Management Actions (REMS):**

Major safety risks have been identified that require a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU). The risks include Cytokine Release Syndrome (CRS) and Neurological Toxicities in the acute phase after treatment. A REMS notification letter was sent to Kite on August 1, 2017. In addition, delayed safety risks have been identified that may include secondary malignancy. Details regarding Kite's proposed patient registry were requested in an August 14, 2017 information request.

**Wrap-up and Action Items**

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.