



Our Reference: BL125643/0

Date: August 16, 2017

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 summary for your July 25, 2017 Mid-Cycle Communication 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 as soon as possible.

Please include a reference to Submission BLA 125643 in your future submissions related to the subject product.

If you have any questions, please contact Mark L. Davidson at (240) 402-8277.

/s/

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

## **Mid-Cycle Communication Teleconference Summary**

**Application type and number:** BL 125643/0

**Product name:** Axicabtagene ciloleucel

**Proposed Indication:** Relapsed/refractory aggressive B-cell NHL

**Applicant:** Kite Pharma, Inc.

**Meeting date & time:** July 25, 2017 2:30pm - 3:30pm EST

**Committee Chair:** Michael Havert, PhD

**RPM:** Mark L. Davidson, RHIA

### **FDA Attendees:**

Mark Davidson, RPM, DRPM/CBER/OTAT  
Najat Bouchkouj, MD, DCEPT/OTAT  
Bindu George, MD DCEPT/OTAT  
Yvette Kasamon, MD, CDER/OHOP/DHP/OCE  
R. Angelo de Claro, MD, CDER/OHOP/DHP/ OCE  
Xiaofei Wang, MD, OMPT/CBER/OBRR  
Xue (Mary) Lin, PhD, CBER/OBE  
Mike Havert, PhD, DCGT/OTAT  
Anna Kwilas, PhD, DCGT/OTAT  
Jakob Reiser, Ph.D., DCGT/OTAT  
Graeme Price, PhD DCGT/OTAT  
Donald Ertel, CMDR, CBER/DMPQ  
Wilson Bryan, MD, OTAT/Director  
Lori Tull, Team Leader, DRPM/CBER/OTAT  
Raj Puri, MD PhD, DCGT/OTAT  
Tejashri Purohit-Sheth, MD, DCEPT/OTAT  
Joyce Weaver, Pharm D, CDER/OSE/OMEPRM/DRISK

### **Applicant Attendees:**

David Chang, MD, PhD, Executive VP Research and Development  
Tim Moore, MS, Executive VP Technical Operations  
Jeff Wiezorek, MD, Senior VP Clinical Development  
Lynn Navale, MS, VP Biometrics  
Rizwana Sproules, MD, VP Regulatory Affairs  
Marc Better, PhD, VP Product Sciences  
Prentice Curry, VP Quality  
David Chonzi, MD, Senior Director, Drug Safety  
Mehrshid Alai-Safar, PhD, Senior Director, Regulatory Affairs  
Nadia Agopyan, PhD, Director, Regulatory Affairs  
Alex Babayan, PhD, Associate Director, Regulatory Affairs

### **Discussion Summary:**

1. Any significant issues/major deficiencies, categorized by discipline, identified by the review committee to date.

#### CMC

We have identified issues regarding proposed shelf life. The stability data does not support the proposed shelf life for the (b) (4) vector and axicabtagene ciloleucel final product. For (b) (4) vector the proposed shelf life is (b) (4), but Kite has not demonstrated (b) (4) beyond (b) (4) of storage. For axicabtagene ciloleucel final product the proposed shelf life is 12 months, but Kite has not demonstrated stability from patient lots in final container beyond 6 months.

**Summary of Discussion:** Kite Pharma stated that they will have additional stability data finalized in July and August and they will submit this information as soon as possible.

We have also identified issues with the post approval stability commitments. For the (b) (4) vector post approval stability commitment, please conduct stability testing according to the schedule provided on samples from each manufacturing campaign (from either (b) (4) lots). For the final product post approval stability commitment, please conduct stability testing on multiple unused patient lots at each time point, as they become available.

**Summary of Discussion:** Kite Pharma is expecting to collect additional stability data on vector and final product lots.

2. Information regarding major safety concerns.

Fatal and life-threatening Cytokine Release Syndrome (CRS) and neurotoxicity events were associated with axicabtagene ciloleucel and are major safety concerns.

Patients exposed to retroviral based CD19 directed CART cell therapy are at risk for long term complications of secondary malignancies.

**Summary of Discussion:** FDA stated it may have additional information requests or may identify additional safety concerns after review of the updated safety information due on July 31, 2017.

3. Preliminary review committee thinking regarding risk management.

The Risk Evaluation and Mitigation Strategy (REMS) is under review. Additional communication regarding the REMS will be sent to the applicant at a later time.

The pharmacovigilance plan for YESCARTA includes a registry of YESCARTA recipients; additional information regarding plans for this registry will be reviewed when submitted and discussed at the time of the late cycle meeting.

4. Any information requests sent and responses not received

CMC

Analytical Method Validation is incomplete, information currently outstanding includes:

- i. Accuracy of axicabtagene ciloleucel viability determination
- ii. Report for axicabtagene ciloleucel (b) (4) validation conducted at (b) (4) (including additional information on samples used)
- iii. Intermediate precision of axicabtagene ciloleucel (b) (4) during assay transfer from (b) (4)
- iv. (b) (4) vector (b) (4) assay: validation of sensitivity and robustness, (b) (4) and additional information on samples used
- v. (b) (4) release assay was validated as if it was a limit test which we do not agree with; requesting further validation
- vi. RCR Test Operator Worksheet (or detailed description of test method) and RCR raw data for (b) (4) lots

5. Any new information requests to be communicated

Efficacy

Regarding ZUMA1 ADTTE.xpt submitted on July 12, for paramcd='PFS\_CS1', three subjects (KTE-C19-101-002-012, KTE-C19-101-009-008 and KTE-C19-101-025-001) received new cancer therapy but were not censored at the last tumor assessment before the new therapy. Please submit an updated ADTTE.xpt with corrected PFS\_CS1 for these three subjects.

6. Proposed date(s) for the Late-Cycle meeting (LCM)

The LCM between you and the review committee is currently scheduled for September 11, 2017 from 1:00 am to 2:00 pm ET.

We intend to send the LCM meeting materials to you approximately 5 business days in advance of the LCM.

If these timelines change we will communicate updates to you during the course of the review.

7. Updates regarding plans for the AC meeting

The Advisory Committee Meeting will not be scheduled.

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.

**External Late-Cycle Meeting:** September 11, 2017

**Labeling Target Date:** October 30, 20107

**PMC Target Date:** October 30, 2017