



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/GTB/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/GTB
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 Cagungun, 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 Wieszorek, 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 ≤ -150 °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.