



Our STN: BL 125643/0

BLA FILING NOTIFICATION

May 25, 2017

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

Dear Dr. Sproule:

This letter is in regard to your biologics license application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated March 31, 2017, for Axicabtagene ciloleucel to determine its acceptability for filing. Under 21 CFR 601.2(a), we have filed your application today. The review classification for this application is **Priority**. Therefore, the review goal date is November 29, 2017. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which include the timeframes for FDA internal milestone meetings. We plan to hold our internal mid-cycle review meeting on July 14, 2017. Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process.

We will contact you regarding your proposed labeling no later than October 30, 2017. If post marketing study commitments (506B) are required, we will contact you no later than October 30, 2017.

At this time, we are still assessing if we will be discussing this application at an Advisory Committee meeting. We expect to notify you of a decision shortly.

While conducting our filing review, we identified the following potential review issues:

1. You have not provided sufficient follow-up to characterize the durability of response. Per the minutes from the October 31, 2016, pre-BLA meeting, "The totality of data, including the ORR, CR, and duration of complete response after

completion of six month follow-up for all subjects, is necessary to assess the efficacy of your product.” We are concerned with the large amount of censoring occurring prior to 6 months in the analyses of duration of response and progression-free survival. We also note that the 6-week difference in data cutoff dates for independent review committee (IRC) and investigator assessments further confounds the interpretation of results.

2. You seek an indication for relapsed/refractory disease (b) (4) [REDACTED]
[REDACTED] You have therefore not established that KTE-C19 is superior to available therapies for (b) (4) refractory disease.
3. You seek an indication for “aggressive B-cell NHL.” However, this is not a World Health Organization diagnosis and the term is overly broad, encompassing many types of lymphoma that were not studied.
4. You seek an indication for patients who are ineligible for autologous Hematopoietic Stem Cell Transplant (HSCT). However, transplant ineligibility was not the entry criterion for ZUMA1 cohorts 1 and 2. The term “ineligible for transplant” is also ambiguous, because reasons for transplant ineligibility include not only comorbidities, but absence of remission. According to the proposed indication, a fit patient with first, untreated relapse could receive KTE-C19 rather than standard salvage chemotherapy, because he has not yet entered the remission typically required for HSCT. This issue also makes the eligibility criteria for ZUMA1 cohort 3 problematic.
5. No rationale was provided for the dose of KTE-C19, and only one target dose was studied in the intended population. As such, the optimal dose of KTE-C19 is not defined.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

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 the indication you are requesting has orphan drug designation, PREA does not apply.

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

Sincerely yours,

Kimberly Benton, Ph.D.
Associate Director for Regulatory Management
Office of Tissue and Advanced Therapies
Center for Biologics Evaluation and Research