Our STN: BL 125646/0

BLA FILING NOTIFICATION
March 28, 2017

Novartis Pharmaceuticals Corporation
Attention: Manisha Patel, PharmD
One Health Plaza, Bldg. 315, Office 3450B
East Hanover, NJ 07936

Dear Dr. Patel:

This letter is in regard to your Biologics License Application (BLA) received on February 2, 2017 under section 351(a) of the Public Health Service (PHS) Act for tisagenlecleucel-T.

We have completed our filing review and have determined that your application dated February 2, 2017, for tisagenlecleucel-T is sufficiently complete to permit a substantive review. Under 21 CFR 601.2(a), we have filed your application today. The review classification for this application is **Priority**, the review goal date is October 3, 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.

This application is also subject to the provisions of "the Program" under the Prescription Drug User Fee Act (PDUFA) (refer to http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm)

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* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079748. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). We plan to hold our internal mid-cycle review meeting on May 8, 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. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by September 1, 2017.

We are currently planning to hold an advisory committee meeting to discuss this application.

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

1. In the pharmacovigilance plan, there are two post-authorization studies referred to in table 7-2 on page 50 of that document. They are listed as follows:

   a. CTL019B2401 Prospective registry to assess long term safety of patients with B lymphocyte malignancies treated with CTL019 (Registry)

   b. CCTL019A2205B Long Term Follow-Up of Patients Exposed to Lentiviral-Based CD19 directed CART Cell Therapy (LTFU study)

   Please provide protocols for those studies (concept protocols are acceptable at this time).

We are providing the above comment to give you preliminary notice of a potential review issue. 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, Erica Giordano, at (240) 402-8298.

Sincerely yours,

Kimberly Benton, PhD
Associate Director for Regulatory Management
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research