T 910.16: FILING MEETING AGENDA/SUMMARY

Application type and number: BL 125646/0
Product name: Tisagenlecleucel-T
Proposed indication: For the treatment of pediatric and young adult patients with relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (ALL)
Applicant: Novartis Pharmaceuticals Corporation
Meeting date & time: March 15, 2017, 2pm – 3pm ET
Meeting Chair: Xiaobin (Victor) Lu, PhD
Meeting Recorder: Erica Giordano

Background: The review team met for the first committee meeting on February 22, 2017

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Manager (RPM)	Erica Giordano	X	X		
Chair	Xiaobin (Victor) Lu, PhD	X	X		
DCGT Division Director DCGT Deputy Director DCEPT Division Director DCEPT Deputy Director	Raj Puri, MD, PhD Steven Oh, PhD Tejashri Purohit-Sheth Ilan Irony	X X X X			
Office Director Office Deputy Director Associate Director for Regulatory Management	Wilson Bryan, MD Rachael Anatol, PhD Kim Benton, PhD	X X X			
Clinical Reviewer	Maura O'Leary, MD	X	X		
Clinical Reviewer	Donna Przepiorka, MD, PhD	X	X		
Toxicology Reviewer	Ying Huang, PhD		X		
CMC Reviewer	Xiaobin (Victor) Lu, PhD	X	X		
CMC Reviewer	Andrew Byrnes, PhD	X	X		
CMC Reviewer	Kimberly Schultz, PhD	X	X		
CMC Reviewer	Elena Gubina, PhD		X		
CMC Reviewer	Tom Finn, PhD		X		
OCBQ/DMPQ RPM	Debra Vause, RN		X		
OCBQ/DMPQ Reviewer	Joan Johnson, MS	X	X		
OCBQ/DMPQ Reviewer	Randa Melhem, PhD	X	X		

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
OCBQ/DMPQ/PRB Reviewer	Cheryl Hulme		X		
OCBQ/APLB Reviewer	Loan Nguyen, PharmD	X	X		
OCBQ/BIMO Reviewer	Dennis Cato	X	X		
OCBQ/DBSQC	Marie Anderson, MS, PhD		X		
OCBQ/DBSQC	Noel Baichoo	X	X		
OCBQ/DBSQC	Simleen Kaur		X		
OCBQ/DMPQ/Lead Inspector	Joan Johnson, MS	X	X		
OCBQ/DMPQ/Lead Inspector	Randa Melhem, PhD	X	X		
CMC Inspector	Xiaobin (Victor) Lu, PhD	X	X		
CMC Inspector	Richard Coats	X	X		
CMC Inspector	Ashley Burns, PharmD	X	X		
CMC Inspector	Kimberly Schultz, PhD	X	X		
Statistical Reviewer of clinical data	Xue (Mary) Lin, PhD	X	X		
Postmarketing Safety Epidemiological/Pharmacologo vigilance Reviewer	Jaspal Ahluwalia,MD	X	X		X
Other Attendee(s)	John Eltermann Jr, RPh, MS	X			
	Anthony Lorenzo	X			
	Bindu George, MD	X			
	Robert Le, MD, PhD	X			
	Becky Robinson, PhD	X			
	Karen Campbell	X			
	Denise Gavin, PhD	X			
	Carrie Mampilly	X			
	Dianne Spillman	X			
	Nannette Cagungun	X			
	Deepa Arya	X			
	Marc Theoret, MD	X			
	Richard Pazdur, MD	X			
	Laurie Norwood	X			
	Tamy Kim	X			
	Ramani Sista, PhD	X			
	Elleni Alebachew	X			
	Geoffrey Kim	X			
	Carolyn Renshaw	X			
	Shiowjen Lee	X			
	Kristin Baird	X			
	Pamela Balcazar, MS	X			

REGULATORY CONCLUSIONS / DEFICIENCIES

1. Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and will require a RTF letter?

Yes, the application is suitable for filing.

2. If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application:

a. Postmarketing Safety Epidemiological/Pharmacologovigilance (OBE/DE) Reviewer – Jaspal Ahluwalia: The PVP refers to a registry for all patients post-approval that will assess long and short terms concerns for AESI, pregnancy, secondary malignancy, vector persistence, B cell aplasia, among other events. The protocol for this registry is not included in the application.

3. If RTF, list any substantive deficiencies or issues that would make this application unsuitable for filing:

None.

FILING MEETING DISCUSSION, IF FILED:

4. Indicate any comments on the status of the proprietary name review (PNR).

APLB is re-evaluating the proprietary name, KYMRIAH. The APLB reviewer will provide an update later in the review cycle. PNR due date is May 3, 2017

5. Indicate whether the product would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.

In the pre-BLA meeting, the FDA stated that tisagenlecleucel-T will be subject to CBER lot release testing. However, we will evaluate the lot release program for the CTL019 during the review of the BLA.

6. Confirm review schedule of this application.

This BLA is being reviewed with priority and expedited review with a target completion date of the end of August/ beginning of September.

7. Indicate the decision regarding the need for an Advisory Committee.

The review committee agreed this BLA should be presented to an advisory committee, tentatively scheduled for July 11, 2017. OHOP has suggested the committee size be limited to around 15 members.

8. Indicate whether the submission triggers PREA; if yes, a PeRC meeting is needed.

This product has received orphan designation and does not trigger PREA. However, BPCA is applicable due to the pediatric exclusivity request. The product is scheduled to go to PeRC on June 7, 2017 to review the written request, and will be discussed by the Pediatric Exclusivity Board (PEB) on June 12, 2017.

9. Is a comprehensive and readily located list of all clinical sites included or referenced in the application?

Yes. Section 5.3.5.4 Data Listing Data; bimo-ctl0199b2202-part1

10. Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?

Yes.

11. Indicate any updates since the First Committee Meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)

BIMO inspectors are in the process of inspecting two foreign clinical sites and four domestic sites are in the process of being scheduled.

DMPQ will conduct one domestic inspection (New Jersey) for the drug product manufacturing operations the first week of April, 2017, and two foreign inspections (b) (4) for the viral vector manufacturing operations in (b) (4)

12. If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

This BLA is not affected by the Application Integrity Policy (AIP).

13. Is the product an Original Biological Product or a New Molecular Entity (NME) for an NDA?

This product is an Original Biological Product

FOR APPLICATIONS IN THE PDUFA PROGRAM (NME NDAs/Original BLAs), IF FILED

14. Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.

6-month follow-up data was provided within 30 days of the original submission.

The CMC vector potency validation data submission has been received.

15. Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?

Yes, the application was relatively complete on submission. Additional information was requested by several disciplines.

ADMINISTRATIVE DETAILS, IF FILED:

16. Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the First Committee Meeting.

With regard to the expedited review, the review schedule will be adjusted based on the target completion date of early September.

BLA Priority 8 Month Review

STN: 125646	
Applicant:	Novartis Pharmaceuticals Corporation
Product:	Tisagenlecleucel-T
Short Summary:	For the treatment of pediatric and young adult patients with relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (ALL)
RPM:	Erica Giordano
Chairperson:	Xiaobin (Victor) Lu

Review Schedule	Target Date
DCC Receipt Date	**Feb 2, 2017**
Complete regulatory filing review; Assign review committee	Feb 10, 2017
Acknowledge receipt; Establish review schedule	Feb 16, 2017
First Committee Meeting	**Feb 23, 2017**
30 Day Late Components Due	*Mar 3, 2017*

Filing Meeting	**Mar 17, 2017**
Send Filing Determination Letter	**Apr 3, 2017**
Deficiencies Identified Letter	Apr 17, 2017
Proprietary Name Review	May 3, 2017
Request initial labeling review	May 5, 2017
Mid-Cycle Review Meeting	**May 19, 2017**
MidCycle Communication with Applicant	Jun 2, 2017
Send Information Requests as needed	
Complete Discipline Reviews (Primary)	**Jun 30, 2017**
Complete Discipline Reviews (Secondary Review)	**Jul 14, 2017**
Send Discipline Review Letters as completed	
Send Late Cycle / Advisory Comm briefing package	Jul 7, 2017
External Late-Cycle Meeting	**Jul 19, 2017**
Advisory Committee Meeting, if needed	**Aug 3, 2017**
Promotional labeling review (APLB)	Jul 5, 2017
Complete inspection reports	Aug 3, 2017
PeRC Meeting	Aug 22, 2017
Circulate draft press release	Sep 1, 2017
Complete PMC Study, Labeling Review, Review Addenda	Sep 1, 2017
Complete Supervisory Review	**Sep 1, 2017**
Request Compliance Check, Lot Release Clearance	Sep 19, 2017
Send Press Release to OCOD	Sep 19, 2017
T-minus date	***Sep 19, 2017***
Send FDA Action Letter	**Oct 3, 2017**

Post-Action Debrief Meeting	Nov 17, 2017