T910.15: First Committee Meeting Agenda/Summary

Application 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: February 22, 2017, 1pm to 2 pm
Committee Chair: Xiaobin (Victor) Lu, PhD
Meeting Recorder: Erica Giordano

Attendees:

Discipline	Name [with credentials (not title)]	Attended meeting?
Regulatory Project Manager (RPM)	Erica Giordano	Y
Chair	Xiaobin (Victor) Lu, PhD	Y
Clinical Reviewer	Maura O'Leary, MD	Y
Clinical Reviewer	Donna Przepiorka, MD, PhD	N
CMC Reviewer	Xiaobin (Victor) Lu, PhD	Y
CMC Reviewer	Andrew Byrnes, PhD	Y
CMC Reviewer	Kimberly Schultz, PhD	Y
CMC Reviewer	Elena Gubina, PhD	N
CMC Reviewer	Tom Finn, PhD	N
Animal Pharmacology Reviewer	N/A	N/A
Clinical Pharmacology Reviewer	N/A	N/A
Toxicology Reviewer	Ying Huang, PhD	N
Developmental Toxicology Reviewer	N/A	N/A
OCBQ/DMPQ RPM	Debra Vause, RN	Y
OCBQ/DMPQ Reviewer	Joan Johnson, MS	Y
OCBQ/DMPQ Reviewer	Randa Melhem, PhD	Y
OCBQ/DMPQ/PRB Reviewer	Cheryl Hulme	N
Statistical Reviewer of clinical data	Xue (Mary) Lin, PhD	Y
Statistical Reviewer of non-clinical data	N/A	N/A
Postmarketing Safety Epidemiological Reviewer	Jaspal Ahluwalia,MD	Y
OCBQ/APLB Reviewer	Loan Nguyen, PharmD	Y
OCBQ/BIMO Reviewer	Dennis Cato	Y
OCBQ/DBSQC Reviewer	Marie Anderson, MS, PhD	Y

Discipline	Name [with credentials (not title)]	Attended meeting?
OCBQ/DBSQC Reviewer	Noel Baichoo	N
OCBQ/DBSQC Reviewer	Simleen Kaur	N
Consult Reviewer(s)	N/A	N/A
OCBQ/DMPQ/Lead Inspector	Joan Johnson, MS	Y
OCBQ/DMPQ/Lead Inspector	Randa Melhem, PhD	Y
CMC Inspector	Xiaobin (Victor) Lu, PhD	Y
CMC Inspector	Richard Coats	N
CMC Inspector	Ashley Burns, PharmD	N
CMC Inspector	Kimberly Schultz, PhD	Y
Labeling Reviewer	N/A	N/A
Other Attendee(s)	Denise Gavin, PhD	Y
	Deepa Arya	Y
	Richard Pazdur, MD	Y
	Marc Theoret, MD	Y
	Gregory Reaman, MD	Y
	Dianne Spillman	Y
	Tamy Kim	Y
	Geoffrey Kim	Y
	Ke Liu	Y
	Kristin Baird	Y
	Shiowjen Lee	Y
	John Eltermann Jr, RPh, MS	Y
	Kim Benton, PhD	Y
	Raj Puri, MD, PhD	Y
	Robert Le, MD, PhD	Y
	Katie Rivers, MS	Y
	Pamela Balcazar, MS	Y
	Rachael Anatol, PhD	Y
	Bindu George	Y
	Ramani Sista, PhD	Y
	Adnan Jaigirdar	Y
	Elleni Alebachew	Y
	Nannette Cagungun	Y
	Carrie Mampilly	Y
	Anthony Lorenzo	Y
	Patricia Holobaugh	Y
	Deborah Trout	Y
	Marie Anderson	Y
	Laurie Norwood	Y
	Albert Deisseroth	Y
	William McCormick	Y

Discussion Summary:

The meeting began with an overview of eMRP by Katie Rivers, a project manager from the eMRP support team. An eMRP demo and hands-on training has been scheduled for the immediate review team for March 6, 2017 from 2 pm to 3:30 pm. (b) (4)

The meeting proceeded with all attendees introducing themselves. The following topics were discussed.

1. Review committee
    a. All discipline reviewers confirmed the above table of review committee members is accurate.
    b. The clinical team explained a clinical pulmonary rheumatology consult reviewer may be needed to provide feedback on labeling.
    c. The CMC team explained a consult reviewer may be needed at a later point in the review cycle.
    d. All discipline reviewers confirmed they have received and are able to access the submission using the provided link.

2. Review schedule
    a. Priority review was confirmed.
    b. Expedited review was discussed but the target completion date is under discussion.
    c. Regular approval was confirmed.
    d. The RPM will establish recurring monthly meetings until the mid-cycle and then weekly meetings will be scheduled. The RPM will poll the review team to find out who wants to be included in these recurring meetings.
    e. The review schedule has been provided below and is tentative based on the target completion date:

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

3. All discipline reviewers confirmed the necessary information is included in the submission – 21CFR601.2. The clinical reviewer explained the sponsor should submit 6-month follow-up data within 30 days of the original submission.

4. The review team confirmed Tisagenlecleucel-T is a PDUFA product.

5. Meetings have been scheduled up to the internal mid-cycle review committee meeting and are tentative based on expedited review and the target completion date.

    a. Walk-through and AOM sponsor meetings – 27Feb17
    b. Filing meeting – 15Mar17
    c. Internal mid-cycle meeting – May 17, 2017

6. FDA Form 3397 is provided in Section 1.1.3. Orphan drug designation was assigned to tisagenlecleucel-T for the treatment of patients with ALL on January 31, 2014 (designation request # 13-4151).

7. PREA is not triggered due to orphan designation. BPCA applies due to the written request. The pediatric exclusivity determination needs to be made within 180 days, by August 1, 2017. Will go to PeRC and the Pediatric Exclusivity Board (PEB) by August 1, 2017.

8. A clinical Advisory Committee (AC) Meeting in the Oncology Drugs Advisory Committee (ODAC) with product participation is likely. The current proposal is for the ODAC to occur between July 11 and July 13, 2017 with the first 2 hours presenting and discussing non-clinical and

manufacturing followed by clinical. The timeline for AC planning would start around March 15, 2017. Potential names for the panel are needed.

9. Potential issues:

    a. CMC – SOPs cannot be located in the submission.
    b. Clinical – A plan for deviation on a product cannot be located in the submission.
    c. Statistical – There is an issue with the wrong 'define' file having been submitted for the pivotal study.
    d. CMC/Facilities –lacking details on equipment and facility qualification data.

10. DMPQ confirmed two inspections covering three sites are planned. One to the (b) (4) for the vector drug substance and to (b) (4) for the vector drug product and the second to the Novartis Morris Plains, New Jersey facility. One additional product office CMC reviewer may be added to the inspection team for the Morris Plains, New Jersey facility. The inspections are tentatively scheduled to occur between (b) (4) depending on the manufacturing schedule.

11. BIMO confirmed six inspections are tentatively scheduled depending on the efficacy data. Two foreign inspections are planned to Spain and Canada and four domestic inspections are planned.

12. Activities to be completed before the Filing Meeting
    a. Discipline reviewers should complete the filing checklist and upload the signed checklist (supervisory concurrence not needed yet) to the BLA SharePoint site by Friday March 10, 2017 by COB
    b. Novartis BL 125646 SharePoint Site
    c. After the filing meeting, reviewers should update their filing checklist if necessary, re-sign, obtain supervisory concurrence and upload the certified checklist to the EDR by March 29, 2017 by COB, 5 days before the filing due date

13. The Filing Meeting is scheduled for March 15, 2017 from 2 pm to 3 pm.
    Be prepared to discuss the relevant content of the application and present an overview that includes:
    a. A summary of the submitted material
    b. A description of any required material that may have been omitted from the application
    c. Any substantive deficiencies or issues that potentially have significant impact on the ability to complete the review or approve the application
    d. Comments on the status of the proprietary name review
    e. A proposal on whether the product would be subject to lot release, surveillance or exempt from lot release per *SOPP 8408.1: Development of Testing Plans and Release of Lots as Part of the Approval Process*

f. A discussion on the need for a RTF or deficiencies identified letter
g. A decision on filing, deficiencies identified or RTF
h. A decision regarding standard or priority review status
i. A decision regarding the need for an Advisory Committee