

Our STN: BL 125714/0

**MID-CYCLE COMMUNICATION
SUMMARY**

April 17, 2020

Juno Therapeutics
Attention: Helen Kim
400 Dexter Avenue N, Suite 1200
Seattle, WA 98109

Dear Ms. Kim:

Attached is a copy of the summary of your March 31, 2020 Mid-Cycle Communication 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 as soon as possible.

Please include a reference to BL 125714/0 in your future submissions related to lisocabtagene maraleucel.

If you have any questions, please contact Mr. Kay Owosela at (240) 402-2667.

Sincerely,

Raj Puri, MD, PhD
Director
Division of Cell and Gene Therapies
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

Mid-Cycle Communication Teleconference Summary

Application type and number: BL 125714/0
Product name: Autologous CD4+ and CD8+ T cells (JCAR017)
Transduced with Self-Inactivating (SIN) Lentiviral Vector (b) (4) Encoding CD19-specific Chimeric Antigen Receptor (CAR) and Truncated Epidermal Growth Factor Receptor (EGFRt); Following Fludarabine and Cyclophosphamide (Isocabtagene maraleucel)
Proposed indication: Treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after at least two prior therapies.
Applicant: Juno Therapeutics
Meeting date & time: March 31, 2020, 4:00-5:00pm ET
Committee Chair: Kimberly Schultz, PhD
RPM: Kay Owosela, MSc, RAC

FDA Attendees:

Meghna Alimchandani, MD, OBE
Rabia Ballica, PhD, OCBQ/DMPQ
Kimberly Benton, PhD, OTAT
Nirjal Bhattarai, PhD, OTAT/DCGT
Wilson Bryan, MD, OTAT
Nannette Cagungun, MS, RAC, PD, OTAT/DRPM
Suzanne Carter, PhD, OCBQ/DMPQ
Dennis Cato, PhD, OCBQ/BIMO
Mei-Yean Chen, MD, CDER/OSE/OMEPRM/DRM
Maryna Eichelberger, PhD, OCBQ/DBSQC
Denise Gavin, PhD, OTAT/DCGT
Andrew Harmon, PhD, OTAT/DCGT
Dana Jones, OCBQ/APLB
Hyesuk Kong, PhD, OCQB/DBSQC
Jiang Liu, PhD, CDER/OTS/OCP/DPM
Tiffany Lucas, PhD, OTAT/DCGT
Narayan Nair, MD, OBE
Manette Niu, MD, OBE
Steven Oh, PhD, OTAT/DCGT
Kay Owosela, MSc, RAC, OTAT/DRPM
Lori Peters, OCBQ/DMPQ
Raj Puri, MD, PhD, OTAT/DCGT
Carolyn Renshaw, OCBQ/DMPQ
Christopher Saeui, PhD, OTAT/DCEPT/PTB
Kimberly Schultz, PhD, OTAT/DCGT
Lisa Stockbridge, PhD, OCBQ/APLB
Marc Theoret, MD, OCE

Deborah Thompson, MD, OBE
Cong Wang, PhD, OBE
Xiaofei Wang, PhD, OTAT/DCEPT

Applicant Attendees:

Helen Kim (Regulatory Affairs)
Wendy Corbett (Regulatory Affairs)
Jennifer Dudinak (Regulatory Affairs)
Joyce Seymour (Regulatory Affairs)
Annie Sturgess (Regulatory Affairs, CMC)
Cheryl Watson (Regulatory Affairs, CMC)
Melanie Eatough (Regulatory Affairs, Labeling)
Daniel Li (Biostatistics)
Mary Mallaney (CMC)
David Fontana (Project Leadership)
Krishnan Vishwanadan (Cell Therapy Franchise)
Stanley Frankel, MD (Clinical Development)
Candice McCoy, MD (Clinical Development)
(b) (6) (Clinical Development)
Ana Kostic, MD (Clinical Development)
Wayne Wallis, MD (Drug Safety and Risk Management)

Discussion:

1. Any significant issues/major deficiencies identified by the Review Committee to date.

a. CMC

Discussions regarding the validation of analytical assays and specifications are ongoing.

b. Clinical

Review issues regarding the rationale for adjudicator's decision was missing in 65 subjects. A teleconference was held on March 19, 2020, and based on the discussion, an IR request was sent on March 26, 2020, requesting additional details pertinent to the adjudicator's assessment.

2. Information regarding major safety concerns.

There are no major safety concerns identified at this time.

3. Preliminary Review Committee thinking regarding risk management.

We have determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of Breyanzi outweigh the risks of Cytokine

Release Syndrome and Neurologic Toxicity. We are reviewing the proposed REMS program for Breyanzi and will be in communication with you regarding the details of the REMS program at a later date.

The pharmacovigilance plan for Breyanzi includes a long-term follow-up registry of Breyanzi recipients; the preliminary protocol is currently under review.

4. Any information requests sent and responses not received.

IR #17 from DMPQ due April 3
IR #19 from Clinical (Efficacy) pending IR #26
IR #22 from CMC due March 31, 2020
IR #24 from Epidemiology due April 1, 2020
IR #25 from Clinical (Safety) due April 1, 2020
IR #26 from Clinical (Efficacy) due April 6, 2020
IR #27 from CMC due April 2, 2020

5. Any new information requests to be communicated.

None.

6. Proposed date for the Late-Cycle Meeting and the Late-Cycle Meeting Materials:

Tuesday, June 2, 2020, 12:30-2:00pm was confirmed by Juno during Mid-cycle communication. This face-to-face meeting may get converted to a teleconference meeting depending on regional safety measures and travel restrictions in response to the COVID-19 pandemic.

7. Updates regarding plans for the AC meeting, if appropriate.

An Advisory Committee meeting is not planned at this time.

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.

All dates are on schedule at the moment but are subject to change based on the COVID-19 pandemic.

9. Discussion of the impact of postponing inspections on the BLA review timeline.

New proposed inspection dates are listed in the table below. An earlier date was requested by Juno for the (b) (4) inspection. The FDA is working with the applicant to determine if an earlier date is feasible.

JuMP Pre-License Inspection	June 15-19, 2020
(b) (4) Pre-License Inspection	(b) (4)

CBER also indicated that we will be requesting documents in advance of the inspection and we would be communicating with them soon regarding this request.

10. Juno's proposed NDC codes.

The proposed NDC codes are acceptable after preliminary review.