



## **LATE-CYCLE MEETING MATERIALS**

Our STN: BLA 125714/0

August 21, 2020

Juno Therapeutics, Inc.  
Attention: Joy Seymour  
400 Dexter Avenue North  
Suite 1200  
Seattle, WA 98109

Dear Ms. Seymour:

Please refer to your Biologic License Application (BLA) submitted under section 351(a) of the Public Health Service Act for for BREYANZI, (lisocabtagene maraleucel), Cell Suspension for Infusion Target 100 x 10e6 CAR-positive viable T cells.

Attached are our meeting materials, including our agenda, for the Late-Cycle Meeting (LCM) scheduled for September 2, 2020 at 12:30PM – 2:00PM, EDT.

If you have any questions, please contact the Regulatory Project Manager, Zakaria Ganiyu at (240) 402 – 8329 / [zakaria.ganiyu@fda.hhs.gov](mailto:zakaria.ganiyu@fda.hhs.gov).

Sincerely,

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

ENCLOSURE:  
Late-Cycle Meeting Materials

## **Late-Cycle Meeting Materials**

**Meeting Date and Time:** September 2, 2020 at 12:20P - 2:00PM, EDT  
**Meeting Location:** Via WebEx (Teleconference)  
**Application Number:** 125714/0  
**Product Name:** lisocabtagene maraleucel  
**Indication:** Treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after at least 2 prior therapies.  
**Applicant Name:** Juno Therapeutics, Inc.

### **INTRODUCTION**

The purpose of a Late-Cycle Meeting (LCM) is to share information and to discuss any substantive review issues that we have identified to date. The application has not yet been fully reviewed by the signatory authorities, division directors, and application Chair. Therefore, the meeting will not address the final regulatory decision for the application. We are sharing this material to promote a collaborative and successful discussion at the meeting.

During the meeting, we may discuss additional information that could be submitted to address any identified issues. We may also discuss whether the submission of such information would be expected to trigger an extension of the PDUFA goal date if the Review Committee should decide, upon receipt of the information, to review it during the current review cycle.

Please note: If you submit any new information in response to the issues identified in this background package prior to this LCM, we may not be prepared to discuss that information at this meeting.

### **SUBSTANTIVE REVIEW ISSUES TO BE DISCUSSED DURING THE LCM**

#### **Division of Manufacturing and Product Quality (DMPQ)**

##### **For Inspections:**

An inspection of the Juno Therapeutics Inc. (FEI# 3011834594, Bothell, WA) and (b) (4) facilities is required before the application can be approved. FDA must assess the ability of these facilities to conduct the listed manufacturing operations in compliance with CGMP. Due to restrictions on travel we may be unable to conduct an inspection of the JuMP (Juno Therapeutics Inc.) and (b) (4) facilities prior to the User Fee Date. We will continue to monitor the public health situation as well as travel restrictions. We are actively working to define an approach for scheduling outstanding inspections, once safe travel may resume and based on public health need and other factors.

For more information, please see the FDA guidances related to COVID 19. These guidances can be found at <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders>

### **ADVISORY COMMITTEE MEETING**

An Advisory Committee meeting is not planned.

### **RISK MANAGEMENT/REMS ACTIONS HAVE BEEN IDENTIFIED**

As communicated previously during the midcycle meeting, FDA has 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 Neurological Toxicity. FDA review is ongoing for your proposed REMS program for lisocabtagene maraleucel.

### **LATE-CYCLE MEETING (LCM) AGENDA**

#### **1. Introductory Comments – 5 Minutes (RPM/Chair)**

Welcome, Introductions, Ground rules, Objectives of the meeting

#### **2. Discussion of Substantive Review Issues – 30 minutes**

Each issue will be introduced by FDA and followed by a discussion.

#### **3. Discussion of Minor Review Issues – 15 minutes**

- a. At the pre-BLA meeting, the FDA agreed to accept an ongoing stability data update within 60 days prior to the PDUFA date. Juno has indicated that the target date for the submission is no later than 17 September 2020. We recommend submitting this information for review as soon as possible, especially given that this agreement was made without consideration for the major amendment.
- b. Commercial lot release acceptance criteria are still under negotiation. Please update the lot release table in BLA in sections 3.2.S.4.1(b) (4) and 3.2.P.5.1 (lisocabtagene maraleucel) after the commercial lot release criteria negotiations are complete.

#### **4. Additional Applicant Data – 10 minutes (Applicant)**

#### **5. Information Requests – 15 minutes**

**6. Postmarketing Requirements/Postmarketing Commitments – 15 minutes**

In amendment 53, received on June 26, 2020 you provided a prospective validation protocol for (b) (4). As discussed on June 19, 2020, this assay validation will be conducted as a post marketing commitment. Should this product be approved, we have determined that an analysis of spontaneous post-marketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to identify a serious risk of secondary malignancies associated with use of lisocabtagene maraleucel. Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess this serious risk. Therefore, should this product be approved, we have determined that you will be required to conduct the following study as a post-marketing requirement (PMR) under Section 505(o) of FDCA: A post-marketing, prospective, multi-center, observational study to assess the long-term safety of lisocabtagene maraleucel and the risk of all secondary malignancies occurring after treatment with lisocabtagene maraleucel. The study will include at least 1000 adult patients with relapsed/refractory large B-cell lymphoma; the enrolled patients will be followed for 15 years after product administration.

We acknowledge the timetable you proposed in the draft protocol for the post-marketing registry study, which includes the following milestones:

- Final protocol submission: January 31, 2021
- Study completion: Q1 2041
- Final study report: Q2 2042

For the above study, please provide dates in mm/dd/yyyy format for Study Completion and Final Report Submission.

**7. Applicant Questions – 10 minutes**

**8. Wrap-up and Action Items – 5 minutes**