



Our STN: BLA 125813/0

**LATE-CYCLE
MEETING MEMORANDUM**

Autolus, Inc.
Attention: Nirav Patel
15810 Gaither Drive,
Suite 230
Gaithersburg, MD 20877

Dear Nirav Patel:

Attached is a copy of the memorandum summarizing your August 2, 2024 Late-Cycle Meeting with CBER. This memorandum constitutes the official record of the meeting. If your understanding of the meeting outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to the appropriate Submission Tracking Number (STN) in future submissions related to the subject product.

If you have any questions, please contact the Regulatory Project Manager, Danielle Bauman at (301) 796 - 4501 or by email at danielle.bauman@fda.hhs.gov.

Sincerely,

Beatrice Kallungal, MS
Director
Division of Review Management and Regulatory Review 1
Office of Review Management and Regulatory Review
Office of Therapeutic Products
Center for Biologics Evaluation and Research

Late-Cycle Meeting Summary

Meeting Date and Time: August 2, 2024, 12:00pm – 1:00pm
Meeting Location: White Oak Campus, Building 71, Room 1208

Application Number: BL 125813
Product Name: obecabtagene autoleucel (obe-cel)
Proposed Indications: Treatment of Adult Patients with Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia (ALL)

Applicant Name: Autolus, Inc.

Meeting Chair: Andrew Timmons, PhD
Meeting Recorder: Danielle Bauman, MPH

FDA ATTENDEES

Meghna Alimchandani, MD, CBER/OBPV/DPV
Pankaj Amin, PhD, CBER/OCBQ/DMP
Rachael Anatol, PhD, CBER/OTP
Kouassi Ayikoe, PhD, CBER/OCBQ/DBSQ 8/06/2024
Danielle Bauman, MPH, CBER/OTP/ORMRR
Najat Bouchkouj, MD, CBER/OTP/OCE
Jessica Chery, PhD, CBER/OTP/OGT
Char-Dell Edwards, CBER/OCBQ/DIS
Mona Elmacken, MD, CBER/OTP/OCE
'Lola Fashoyin-Aje, MD, MPH, CBER/OTP/OCE
Feorillo Galivo, MD, PhD, CBER/OTP/OPT
Harry Houghton, MS, CBER/OBPV/DB
Kula Jha, PhD, CBER/OCBQ/DMPQ
Beatrice Kallungal, MS, CBER/OTP/ORMRR
Timothy Kamaldinov, PhD, CBER/OTP/OGT
George Kastanis, MS, CBER/OCBQ/DBSQ
Wei Liang, PhD, CBER/OTP
Tiffany Lucas, PhD, CBER/OTP/OGT
Lori Peters, CBER/OCBQ/DMPQ
Graeme Price, PhD, CBER/OTP/OGT
Donna Przepiorka, MD, PhD, CDER/OND/OOD/DHMI
Kimberly Schultz, PhD, CBER/OTP/OGT
Anurag Sharma, PhD, CBER/OTP/OGT
Ramani Sista, PhD, CBER/OTP/ORMRR
Lisa Stockbridge, PhD, CBER/OCBQ/DCM/APLB
Deborah Thompson, MD, MSPH, CBER/OBPV/DPV
Andrew Timmons, PhD, CBER/OTP/OGT
Nicole Verdun, MD, CBER/OTP

Cong Wang, PhD, CBER/OBPV/DB
Xiaofei Wang, PhD, CBER/OTP/OCE
Kerry Welsh, CBER/OBPV/DPV

APPLICANT ATTENDEES

Siddhartha Bhaumik - Senior Director, Analytical Development
Edgar Braendle, Clinical Consultant
Andrea Braun, SVP, Head of Global Regulatory Affairs
Wolfram Brugger, VP, Head of Clinical Development
Rahul Chandrasekhar, Associate Director, Regulatory Affairs
Monica Commerford, Executive Director, Head of CMC Regulatory Affairs
Elaine Dymond, VP, Quality Leadership
Markus Gruell, VP, Head of Quality
Mohammad Khalil, VP, Drug Safety & Pharmacovigilance
Koki Lilova, VP, Process Research
Michael Merges, VP, Process Development
Miranda Neville, SVP, Program and Portfolio Management
Nirav Patel, Senior Director, Regulatory Affairs
Cara Romanowski, Senior Manager, CMC Regulatory Affairs
Joana Torres, Associate Director, CMC Regulatory Affairs
Michael Zhang, VP, Head of Biometrics

BACKGROUND

BLA125813/0 was submitted on November 17, 2023, for obecabtagene autoleucel (obecel)

Proposed indication: Treatment of Adult Patients with Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia (ALL)

PDUFA goal date: November 16, 2024

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on July 23, 2024.

DISCUSSION

1. Discussion of Substantive Review Issues

No substantive review issues have been identified at this time.

Meeting Discussion:

No discussion during the meeting.

2. Discussion of established Pharmacologic Class

- a. Proper name - obecabtagene autoleucel (obe-cel)
- b. CD19-directed genetically modified autologous T cell immunotherapy

Meeting Discussion:

No discussion during the meeting.

3. Discussion of Minor Review Issues

a. Clinical:

We plan to ask you to submit updated efficacy and safety datasets based on FDA's adjudication. Issues will be addressed through information requests (IR) and during labeling negotiations.

Meeting Discussion:

The Applicant asked the Agency to provide an estimated timeframe for when they can expect the Agency's adjudication. The Agency stated that the review team will issue the clinical IR later today (8/2/2024) and request a two-week turnaround for the response.

b. CMC:

- i. Based on updated stability information (provided in response to CMC IR #6 on 19-Jul-2024), you have not yet justified a stability shelf life of 6 months for the obe-cel drug product. Please submit additional stability data no later than 17-Sep-2024 (i.e., 60 days prior to the action due date) to justify a stability shelf life of 6 months.
 - o No discussion for this item
- ii. We do not agree with certain acceptance criteria defined in Modules 3.2.S.4.5 and 3.2.P.5.6. Updating these acceptance criteria will be addressed in a subsequent CMC IR.

Meeting Discussion:

The Agency has indicated that an additional information request will be issued regarding certain acceptance criteria provided in Sections 3.2.S.4.5 and 3.2.P.5.6. The Applicant asked the Agency to please clarify which

specific acceptance criteria will be within the scope of the planned information request. The Agency indicated that the acceptance criteria of primary concern relates to the viability of the obe-cel drug product; however, the IR will not be limited to viability. With respect to viability, the current specification of (b) (4) is not reflective of their experience in the clinical study. The viability specification will be addressed in a CMC IR, as this has additional impacts on the evaluation of your stability study.

4. Information Requests

- a. DMPQ: IRs #7 and #8 were sent to Applicant on July 22, 2024 with a response due on July 30, 2024.
- b. Additional IRs will be requested as needed.

*Post-agenda update provided at meeting:

- Informal meeting scheduled for August 7 to discuss DMPQ IR#7
- Response to IR #8 received July 30, 2024
- DMPQ IR #9 sent; response due on August 7, 2024

Meeting Discussion:

No discussion during the meeting.

5. Risk Management Actions (e.g., REMS, the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk)

We have determined that REMS will not be required. The review is ongoing; the need for PMRs or PMCs remains undetermined at this time.

Meeting Discussion:

The Agency has determined that a REMS will not be required. The Applicant asked if the Agency will be issuing a formal IR requesting revisions to the pharmacovigilance (PV) plan to appropriately reflect this. The Agency requested the Applicant submit an updated PV plan to appropriately reflect that a REMS will not be required; a formal IR will also be issued. The Applicant also asked if the Agency could confirm whether the draft REMS materials submitted to the BLA can be deleted from the BLA eCTD dossier. The Agency responded that the Applicant's proposed REMS would not be deleted from the eCTD as it was part of the original BLA submission and was reviewed by FDA.

6. Postmarketing Requirements/Postmarketing Commitments

- a. Office of Biostatistics and Pharmacovigilance (OBPV) - review of the pharmacovigilance plan and protocol synopsis for the postmarketing long-term follow-up registry study are ongoing. We will communicate in the future regarding any potential safety-related PMRs/PMCs.

- b. Clinical- We will communicate in the future regarding the Pediatric Research Equity Act (PREA) PMR for molecularly targeted pediatric cancer investigations.

Meeting Discussion:

The Applicant informed the Agency of the ongoing pediatric study in the US, UK and Spain. The AUTO1-PY1 pediatric clinical study is a single-arm, open-label, multi-center, Phase Ib study evaluating the safety and efficacy of obe-cel in pediatric patients with relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B ALL) and aggressive mature B-cell non-Hodgkin lymphoma (B NHL). This study is also reflected in the agreed iPSP. The Agency stated that the review team is aware of the ongoing pediatric study as per the agreed iPSP and will communicate with the Applicant the PREA PMR language as per the timeline listed below.

7. Major Labeling Issues

Labeling issues will be communicated during the labeling negotiations.

Meeting Discussion:

No discussion during the meeting.

8. Review Plans

- a. Anticipated PMRs will be communicated no later than September 20, 2024.
- b. Proposed PMRs/PMCs will be communicated no later than October 17, 2024.
- c. Label negotiations will begin no later than October 17, 2024.
- d. PDUFA Action Due Date is Saturday, November 16, 2024

Meeting Discussion:

No discussion during the meeting.

9. Applicant Questions

Meeting Discussion:

The Applicant asked the Agency to confirm that all GCP and GMP facility inspections have concluded. The Agency confirmed all GCP and GMP facility inspections have concluded.

10. Wrap-up and Action Items

- Clinical team will provide an information request (IR) regarding the Agency's adjudication by the end of the day (Agency provided IR on August 2, 2024).

- Office of Biostatistics and Pharmacovigilance (OBPV) will submit a formal information request requesting a revised PV plan but asks that the Applicant submitted REMS remain in the eCTD dossier due to the Agency's review of the original submission (Agency provided IR on August 2, 2024).

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.