



Our STN: BL 125788/0

**LATE-CYCLE
MEETING MEMORANDUM**

bluebird bio, Inc.
Attention: Megan Parsi, MBS
455 Grand Union Boulevard
Somerville, MA 02145

Dear Ms. Parsi:

Attached is a copy of the memorandum summarizing your October 6, 2023, Late-Cycle 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 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, Linda Le, by email at Linda.Le@fda.hhs.gov.

Sincerely,

Mara Miller, MA
Director
Division of Review Management and Regulatory Review 2
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: October 6, 2023 | 9:30 AM – 11:30 AM, EST
Meeting Location: Teleconference via Zoom
Application Number: BLA 125788/0
Product Name: lovotibeglogene autotemcel
Proposed Indications: Treatment of patients 12 years of age or older with sickle cell disease and a history of vaso occlusive events (VOEs).
Applicant Name: bluebird bio, Inc.
Meeting Chair: Graeme Price, PhD, CBER/OTP/OGT
Meeting Recorder: Linda Le, MBA, CBER/OTP/ORMRR

FDA ATTENDEES:

Ritu Agarwal, PhD, CBER/OCBQ/DBSQC
Maureen DeMar, BSN, RN, CBER/OCBQ/DMPQ
Esmeralda Alvarado Facundo, PhD, CBER/OCBQ/DBSQC
Alan Baer, PhD, CBER/OTP/OGT
Claire Wernly, PhD, CBER/OCBQ/DBSQC
Zhong Gao, PhD, CBER/OBPV/DB
Denise Gavin, PhD, CBER/OTP/OGT
Christine Harman, PhD, OCBQ/DMPQ
Marisa Gillies, CBER/OTP/ORMRR
Leyish Minie, MSN, RN, CBER/OTP/ORMRR
Edward Thompson, CBER/OTP/ORMRR
Lin Huo, PhD, CBER/OBPV/DB
Megha Kaushal, MD, CBER/OTP/OCE
Harry Houghton, MS, CBER/OBPV/DB
Christine Knoll, MD, CBER/OTP/OCE
Anna Kwilas, PhD, CBER/OTP/OGT
Anthony Lorenzo, CBER/OCBQ/DMPQ
Zainab Mansaray-Storms, PhD, CBER/OCBQ/DMPQ
Prasad Mathew, MD, CBER/OTP/OCE
Mara Miller, MA, CBER/OTP/ORMRR
Shiowjen Lee, PhD, CBER/OBPV/DB
Graeme Price, PhD, CBER/OTP/OGT
Carolyn Renshaw, CBER/OCBQ/DMPQ
Kimberly Schultz, PhD, CBER/OTP/OGT
Marie Anderson, PhD, CBER/OCBQ/DBSQC
John Scott, PhD, MA, CBER/OBPV/DB
Muhammad Shahabuddin, CBER/OCBQ/DBSQC
Ramani Sista, PhD, CBER/OTP/ORMRR
Lisa Stockbridge, PhD, CBER/OCBQ/DCM/APLB
Brian Stultz, MS, CBER/OTP/OGT
Andrew Timmons, PhD, CBER/OTP/OGT

Sakshi Tomar, PhD, CBER/OTP/OPT
Melek Sunay, PhD, CBER/OTP/OPT
Ashley Munchel, MD, CBER/OTP/OCE
Nicole Verdun, MD, CBER/OTP
Meghna Alimchandani, MD, CBER/OBPV/DPV
Peter Lenahan, DC, PhD, MPH, CBER/OCBQ/DIS
Christopher Trindade, MD, CDRH/OPEQ/OHT7
Xiaofei Wang, PhD, CBER/OTP/OCE
Kerry Welsh, MD, PhD, CBER/OBPV/DPV
Lihan Yan, PhD, CBER/OBPV/DB

APPLICANT ATTENDEES:

Anjulika Chawla, MD, Clinical Research Development
Rich Colvin, MD, CMO
Marc d'Anjou, MSc, Regulatory Science, CMC
(b) (4), Regulatory Strategy, consultant
Marisa Gayron, MS, Biometrics, Head
Matt Hibbert, Regulatory Science, CMC
(b) (4), Regulatory Strategy, consultant
Ankit Lodaya, MS, Pharmacovigilance
Suzie Melotti, BSc., MBA, CMC Lead, Process Development
Lin Pan, MS, Biostatistics
Megan Parsi, MBS, Regulatory Strategy, Head
John Pierciey, MS, Research, Head
Ajay Singh, MD, Pharmacovigilance, Head
Tito Suarez, Regulatory Science, CMC
Himal Thakar, MD, Clinical Research Development, Head
Leslie Wilder, MS, Regulatory Science, Head

BACKGROUND

BLA 125788/0 was submitted on April 21, 2023, for lovotibeglogene autotemcel.

Proposed indication: Treatment of patients 12 years of age or older with sickle cell disease and a history of vaso occlusive events (VOEs).

PDUFA goal date: December 20, 2023

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on September 26, 2023.

DISCUSSION

1. Discussion of established Pharmacologic Class
 - a. Autologous Hematopoietic Stem-Cell-Based Gene Therapy

Meeting Discussion:

The FDA confirmed the established Pharmacologic class will be an “Autologous Hematopoietic Stem-Cell-Based Gene Therapy”. The applicant had no further questions.

2. Discussion of Minor Review Issues

Chemistry, Manufacturing, and Controls (CMC):

- a. BB305 lentiviral vector (LVV) stability and lovo-cel DP stability: Stability information is under review. Expiry dates for BB305 and lovo-cel DP are yet to be determined. Please provide any stability updates no later than 60 days before the action due date (ADD), i.e., October 20, 2023.

Meeting Discussion:

The FDA noted that the stability data submitted and received on August 14, 2023, is still under review. The FDA requested and reiterated that additional stability data should be submitted by the Applicant no later than 60 days before the action due date (October 20, 2023). The Applicant acknowledged the FDA’s request and will submit the additional Stability data by October 20, 2023, as a formal amendment to the BLA.

Clinical:

- b. The efficacy data with the data cutoff of February 13, 2023 as submitted in Clinical IR #5 dated August 29, 2023, will be included in the review and label.

Meeting Discussion:

The FDA reiterated that the efficacy data with the data cutoff date of February 13, 2023, submitted in Clinical IR #5 dated August 29, 2023, will need to be included in the review and label. The Applicant acknowledged the FDA’s request and will include the most recent efficacy data in the label.

3. Information Requests

At this time, there are no pending IRs. As our review continues, new information requests will be conveyed as needed.

Meeting Discussion:

There was no discussion of this item during the meeting.

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

The review is ongoing. The need for a Risk Evaluation and Mitigation Strategy (REMS), PMRs, or PMCs remains undetermined at this time.

Meeting Discussion:

The FDA confirmed the review is still ongoing, and the need for Risk Evaluation and Mitigation Strategy (REMS), PMRs, or PMCs remains undetermined at this time. The Applicant requested that the FDA communicate any REMS, PMRs, or PMCs as soon as possible.

5. Postmarketing Requirements/Postmarketing Commitments

Chemistry, Manufacturing, and Controls (CMC):

- a. The review is ongoing. The need for post-marketing requirements (PMRs) or post-marketing commitments (PMCs) remains undetermined at this time.

Clinical/Epidemiology:

- b. The review is ongoing. The need for PMRs or PMCs remains undetermined at this time.

Meeting Discussion:

There was no discussion of this item during the meeting. Please refer to item #4.

6. Major Labeling Issues

- a. Label review is ongoing. Any labeling issues will be discussed during the labeling negotiations.

Meeting Discussion:

The FDA confirmed any labeling issues will be communicated and discussed during the labeling negotiations.

7. Review Plans

- a. PMRs will be communicated no later than November 8, 2023, if needed
- b. PMCs will be communicated no later than November 20, 2023, if needed
- c. Label will be sent to Applicant for negotiations no later than November 20, 2023

Meeting Discussion:

The FDA confirmed the above review dates for the remainder of the review cycle.

8. Applicant Questions

The Applicant asked if there were any additional concerns regarding insertional oncogenesis from DPV IR#1 dated July 31, 2023.

FDA acknowledged that we have noted the Applicant's rationale for insertional oncogenesis as an important potential risk. The FDA stated that the safety specifications in the pharmacovigilance plan (PV) may be updated in the future as we continue our review for this product. However, the FDA does not have further comments as the review is still ongoing. FDA will address any questions through information requests and will request informal teleconferences to address any concerns as needed.

9. Wrap-up and Action Items

Meeting Discussion:

FDA reiterated any PMRs will be communicated to the Applicant no later than November 8, 2023, and any PMCs will be communicated no later than November 20, 2023. The label will be sent to the Applicant for negotiations by November 20, 2023. The FDA confirmed the meeting summary will be provided to bluebird bio within 30 days.

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.