



Our STN: BL 125788/0

**MID-CYCLE COMMUNICATION
SUMMARY**
September 12, 2023

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

Dear Ms. Parsi:

Attached is a copy of the summary of your August 15, 2023, 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 STN BL 125788/0 in your future submissions related to lovotibeglogene autotemcel.

If you have any questions, please contact 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

Mid-Cycle Communication Teleconference Summary

Application Type and Number: BLA 125788/0
Product Name: lovotibeglogene autotemcel
Proposed Indication for Use: Treatment of patients 12 years of age or older with sickle cell disease and a history of vaso occlusive events (VOEs).
Applicant: bluebird bio, Inc.
Meeting Date & Time: August 15, 2023 | 3:00 PM – 4:30 PM (ET)
Committee Chair: Graeme Price, PhD, CBER/OTP/OGT
RPM: Linda Le, MBA, CBER/OTP/ORMRR

FDA Attendees:

Meghna Alimchandani, MD, CBER/OBPV/DPV
Marie Anderson, PhD, CBER/OCBQ/DBSQC
Takele Argaw, DVM, MSc, CBER/OTP/OGT
Alan Baer, PhD, CBER/OTP/OGT
Danielle Bauman, CBER/OTP/ORMRR
Dennis Cato, CBER/OCBQ/DIS/BMB
Maureen DeMar, BSN, RN, CBER/OCBQ/DMPQ
Esmeralda Alvarado Facundo, PhD, CBER/OCBQ/DBSQC
Zhong Gao, PhD, CBER/OBPV/DB
Leila Hann, CBER/OTP
Christine Harman, PhD, OCBQ/DMPQ
Harry Houghton, MS, CBER/OBPV/DB
Megha Kaushal, MD, CBER/OTP/OCE
Christine Knoll, MD, CBER/OTP/OCE
Carolyn Laurencot, PhD, CBER/OTP/OCTHT
Linda Le, MBA, CBER/OTP/ORMRR
Shiowjen Lee, PhD, CBER/OBPV/DB
Peter Lenahan, DC, PhD, MPH, CBER/OCBQ/DIS
Wei Liang, PhD, CBER/OTP
Anthony Lorenzo, CBER/OCBQ/DMPQ
Zainab Mansaray-Storms, PhD, CBER/OCBQ/DMPQ
Prasad Mathew, MD, CBER/OTP/OCE
Leyish Minie, MSN, RN, CBER/OTP/ORMRR
Kavita Natrajan, MD, CBER/OTP/OCE
Graeme Price, PhD, CBER/OTP/OGT
Carolyn Renshaw, CBER/OCBQ/DMPQ
Kimberly Schultz, PhD, CBER/OTP/OGT
Ramani Sista, PhD, CBER/OTP/ORMRR
Lisa Stockbridge, PhD, CBER/OCBQ/DCM/APLB
Brian Stultz, MS, CBER/OTP/OGT
Melek Sunay, PhD, CBER/OTP/OPT
Edward Thompson, CBER/OTP/ORMRR
Deborah Thompson, MD, MSPH, CBER/OBPV/DPV

Nicole Verdun, MD, CBER/OBRR
Xiaofei Wang, PhD, CBER/OTP/OCE
Kerry Welsh, MD, PhD, CBER/OBPV/DPV
Claire H. Wernly, PhD, CBER/OCBQ/DBSQC
Lihan Yan, PhD, CBER/OBPV/DB

Applicant Attendees:

Melissa Bonner, Research, Head (interim)
Anjulika Chawla, MD, Clinical Research Development
Marc d'Anjou, MSc, Regulatory Science, CMC
(b) (4), Regulatory Strategy
(b) (4), Regulatory Project Management
Matt Hibbert, Regulatory Science, CMC
(b) (4), Regulatory Strategy
Ankit Lodaya, MS, Pharmacovigilance
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

Agenda:

Discussion Summary:

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.
 - a. The review is ongoing. There are no significant issues/major deficiencies identified at this time.

Meeting Discussion:

No further discussion.

2. Information regarding major safety concerns.

Clinical

- a. Our primary concern is the risk of hematologic malignancy that has occurred when receiving this therapy.
- b. Delayed Platelet engraftment.

Meeting Discussion:

FDA stated two safety concerns identified by the Clinical review team. FDA noted that the responses to the Clinical Information Requests are currently still under review. FDA will address any questions through Information Requests and will request informal teleconferences to address any concerns as needed.

3. Preliminary Review Committee thinking regarding a) risk management, b) the potential need for any post-marketing requirement(s) (PMRs), and c) the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk.
 - a. The review is ongoing. The need for Risk Evaluation and Mitigation Strategy (REMS), PMR or PMC remains undetermined at this time.

Meeting Discussion:

No further discussion.

4. Any information requests sent, and responses not received.
 - a. CMC IR #2 sent August 8, 2023, due August 14, 2023.

Meeting Discussion:

FDA noted the response to this Information Request was received by the Agency and that the review is still ongoing. The applicant may anticipate additional Information Requests as review progresses.

5. Any new information requests to be communicated.
 - a. As our review continues, new information requests will be conveyed as needed.

Meeting Discussion:

No further discussion.

6. Proposed date for the Late-Cycle meeting (LCM).
 - a. The LCM with the Review Committee is currently scheduled for Friday, October 6, 2023, from 9:30AM – 11:30AM (ET). We intend to send the LCM meeting materials to you by September 26, 2023.

If these timelines change, we will communicate updates to you during the course of the review.

Meeting Discussion:

No further discussion.

7. Updates regarding plans for the AC meeting.

- a. An Advisory Committee (AC) will not be scheduled for BLA 125788/0.

Meeting Discussion:

No further discussion

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates, and notification of intent to inspect manufacturing facilities.

- | | |
|-----------------------------------------------|-------------------|
| a. External Mid-Cycle Meeting with Applicant | August 15, 2023 |
| b. External Late-Cycle Meeting with Applicant | October 6, 2023 |
| c. Communicate Anticipated PMRs | November 8, 2023 |
| d. Communicate Proposed Labeling and PMCs | November 20, 2023 |
| e. Send FDA Action Letter | December 20, 2023 |

Inspection Schedule:

- a. Inspection of (b) (4) is scheduled for (b) (4).
- b. Inspection of (b) (4) is scheduled for (b) (4).
- c. Three U.S. Clinical Investigator Site Inspections were selected.

Meeting Discussion:

The Applicant inquired if the Agency could provide the list of Clinical Investigator sites that will be inspected for the BLA review. FDA responded that the Office of Regulatory Affairs (ORA) generally provides ample notification of Clinical Investigator inspection when the site visit is pre-announced.

End