



Our STN: BL 125807/0

**LATE-CYCLE
MEETING MEMORANDUM**
March 27, 2024

Abeona Therapeutics, Inc.
Attention: Carl Denny
Vice President, Regulatory Affairs
6555 Carnegie Ave, 4th Floor
Cleveland, OH 44103

Dear Carl Denny:

Attached is a copy of the memorandum summarizing your March 21, 2024, Late-Cycle Meeting with CBER. This memorandum constitutes the official record of the meeting. If your understanding of the meeting outcome 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 STN BL 125807 in future submissions related to the subject product.

If you have any questions, please contact Hawa Camara at hawa.camara@fda.hhs.gov, or at (240) 402-8097.

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: March 21, 2024; 11:00 AM – 12:00 PM EST
Meeting Location: Zoom and In-person at FDA White Oak Campus
Application Number: BL 125807/0
Product Name: prademagene zamikeracel
Proposed Indications: Treatment of wounds associated with recessive dystrophic epidermolysis bullosa (RDEB)
Applicant Name: Abeona Therapeutics, Inc.
Meeting Chair: Bao-Ngoc Nguyen, PhD
Meeting Recorder: Hawa Camara, MS, PMP

FDA ATTENDEES

Meghna Alimchandani, MD, CBER/OBPV/DPV
Rachael Anatol, PhD, CBER/OTP
Ritu Argawal, CBER/OCBQ/DBSQC
Kenisha Atkins, MS, CBER/OTP/ORMRR
Colleen Caldwell, MS, MPH, CBER/OTP/ORMRR
Hawa Camara, MS, PMP, CBER/OTP/ORMRR
Dennis Cato, CBER/OCBQ/DIS
Yang Chang, PhD, PharmD, CBER/OTP/OCE
Haecin Chun, MS, CBER/OCBQ/DIS
Brianna Davis, CBER/OCBQ/DBSQC
Denise Gavin, PhD, CBER/OTP/OGT
Alifiya Ghadiali, CBER/OCBQ/DMPQ
Christine Harman, PhD, OCBQ/DMPQ
Alicia Howard, CBER/OCBQ/DBSQC
Guo-Chiuan Hung, PhD, CBER/OTP/OGT
Gavin Imperato, MD, PhD, CBER/OTP/OCE
Simleen Kaur, MSc, CBER/OCBQ/DBSQC
James Kenney, CBER/OCBQ/DBSQC
Joshua Kufera, PhD, CBER/OTP/OGT
Vijay Kumar, MD, CBER/OTP/OCE
Carolyn Laurencot, PhD, CBER/OTP/OCTHT
Shiowjen Lee, PhD, CBER/OBPV/DB
Wei Liang, PhD, CBER/OTP
Heather Lombardi, PhD, CBER/OTP/OCTHT
Anthony Lorenzo, CBER/OCBQ/DMPQ
Ou Ma, CBER/OCBQ/DMPQ
Ileana Marrero-Berrios, PhD, CBER/OTP/OCTHT
Mo Liu, PhD, CBER/OTP/OGT
Bao-Ngoc Nguyen, PhD, CBER/OTP/OCTHT
Steven Oh, PhD, CBER/OTP/OCTHT
Chinwe Okoro, MD, CBER/OTP/OCE

Sarada Panchanathan, MD, CBER/OBPV/DPV
Carolina Panico, MD, PhD, CBER/OTP/OCTHT
Lori Peters, CBER/OCBQ/DMPQ
CDR Kenneth Phillips, CBER/OCBQ/DBSQC/LAC
Graeme Price, PhD, CBER/OTP/OGT
Carolyn Renshaw, CBER/OCBQ/DMPQ
Laura Ricles, PhD, CBER/OTP/OCTHT
Helen Sansone, CBER/OTP/ORMRR
Kimberly Schultz, PhD, CBER/OTP/OGT
John Scott, PhD, MA, CBER/OBPV/DB
Ramani Sista, PhD, CBER/OTP/ORMRR
Theodore Stevens, MS, RAC, CBER/OTP
Brian Stultz, MS, CBER/OTP/OGT
Amanda Szucsik, DVM, MS, CBER/OTP/OPT
Zehra Tosun, PhD, CBER/OTP/OCTHT
Nicole Verdun, MD, CBER/OTP
Kerry Welsh, CBER/OBPV/DPV
Boguang Zhen, PhD, CBER/OBPV/DB
Tingting Zhou, PhD, CBER/OBPV/DB
Iryna Zubkova, PhD, CBER/OCBQ/DMPQ

APPLICANT ATTENDEES

Dr. Vishwas Seshadri, Chief Executive Officer, Abeona Therapeutics Inc (Abeona)
Carl Denny, Sr. Vice President, Head of Regulatory Affairs, Abeona
Kate Imhoff, Vice President, Regulatory Affairs, Abeona
Kysler De Guzman, Executive Director, Regulatory Affairs CMC, Abeona
Steven La, Associate Director, Regulatory Affairs, Abeona
Dr. Brian Kevany, Sr. VP, Chief Technical Officer & Chief Scientific Officer, Abeona
Dr. Ann Durbin, Senior Director, Assay Development, Abeona
Dr. Clarisse Rogat, Director, Process Development, Abeona
(b) (6) Senior Scientist, Assay Development, Abeona
Megan Callan, Executive Director, Head of Quality, Abeona
Curtis Bordwell, Associate Director, Quality Control, Abeona
Dr. Dmitriy Grachev, Chief Medical Officer, Abeona
Amanda Moore, Vice President, Head of Program Leadership & Operations, Abeona
(b) (4), (b) (6) Head of Biometrics, Consultant
Ryan Wolford, Director, Manufacturing, Abeona
Dr. Jean Tang, Lead Investigator for EB-101 Clinical Trials
Angela Iheanacho, Director, Clinical Operations, Abeona
(b) (4), (b) (6) Principal Statistician, Consultant
Shelby Davis, Director, Program Leadership, Abeona
Scott Kerns, Sr. Manager, Program Leadership, Abeona
Scott Arnott, Manager, Quality Operations, Abeona
Aaron Cardinal, Director, Validation, Abeona
(b) (4), (b) (6) Regulatory Consultant

Dr. Paul Wille, Director, Head of Nonclinical Research

(b) (4), (b) (6) Sen. Reg. Device & Biologics Expert, (b) (4)
(b) (4)

BACKGROUND

BLA 125807 was submitted on September 25, 2023, for prademagene zamikeracel.

Proposed indication: Treatment of wounds associated with recessive dystrophic epidermolysis bullosa (RDEB)

PDUFA goal date: May 25, 2024

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on March 11, 2024.

DISCUSSION

1. Discussion of Substantive Review Issues

The following substantive review issues have been identified to date:

Chemistry, Manufacturing, and Controls (CMC)

- a. Safety concerns remain with the revised sterility assurance plan provided as supplemental information to IR #15 (CMC IR#7), received February 8, 2024. While the revised plan includes improvements to the sterility test methods (e.g., inclusion of a rapid sterility testing method, (b) (4) of media test sample with DP), we still have the following concerns (please refer to IR #30 (CMC IR#12), dated March 6, 2024):
 - i. It is unclear if the new test sample (i.e., (b) (4) (b) (4) (b) (4) is adequate to allow for detection of contamination in the DP. (b) (4) studies are necessary to demonstrate adequacy of the sterility test sample for all assays utilizing this test sample (i.e., rapid sterility testing, endotoxin, (b) (4)
 - ii. The validation of the rapid sterility test method has not been completed but is required prior to commercialization to support sterility assurance of the final drug product.
 - iii. Sterility testing, per (b) (4) on the final drug product is not included in the revised sterility testing plan. This testing is necessary to ensure final product sterility using a (b) (4) assay.

- b. A product-specific RCR validation study has not been performed for testing of the (b) (4) as identified in your IR response to CMC IR#11. You indicated that you are “in the process of identifying a CRO that can perform the RCR validation activity.” However, the validation testing plan and timeline for completion of the validation testing are unclear. This test is necessary to demonstrate safety of the (b) (4). We note that this assay is currently performed at (b) (4). Please clarify whether you intend to use a different CRO for this vector release testing.
- c. In response to a CMC IR #10 Question 4, you proposed to develop a characterization test for keratinocyte identity testing “using a (b) (4) (b) (4) method.” Currently, the identity testing involves (b) (4) (b) (4). However, no (b) (4) is performed. Additional information is needed regarding the additional identity testing method, including acceptance criteria with justification, and a timeline for validation of the method.

Meeting Discussion:

FDA provided an overview of the remaining substantive deficiencies, as outlined in the meeting agenda, reiterating that the final validation reports for the safety assays (i.e., sterility and RCR testing) should be submitted prior to approval of the BLA.

Abeona discussed their revised sterility assurance plan, indicating the use of a (b) (4) assay as well as a rapid sterility assay, along with endotoxin, (b) (4) and (b) (4) testing. Abeona indicated that the final validation reports would be provided to FDA for review by end of August 2024. FDA acknowledged Abeona’s proposal and response, and clarified that (b) (4) (b) (4) as well as rapid sterility testing would require separate validations, as they are considered two separate assays. Abeona acknowledged that they understood.

When prompted by FDA, Abeona confirmed that as part of their (b) (4) (b) (4) they plan to include (b) (4) as well as (b) (4). FDA indicated that such inclusion would classify the assay as a sterility assay.

Next, Abeona presented their plans for contracting a new Contract Research Organization (CRO) to conduct the (b) (4) testing on the (b) (4) including the validation of this new method. Abeona proposed to provide the final validation report by April 2025. FDA acknowledged the new (b) (4) test method plans but expressed concern with the information provided on the current (b) (4) method validation. Specifically there is insufficient product-specific information, including (b) (4) assessment, which will impact (b) (4) available for commercial use. Abeona responded that they only have enough material for the feasibility runs, but not enough to complete a validation. Abeona acknowledged that they need to generate more material for validation purposes. FDA stated

that additional product-specific information to support the current (b) (4) assay method, such as sensitivity data from a (b) (4) control to assess the current method matrix effect, is necessary prior to approval.

Regarding Abeona's plan to evaluate identify of the final DP using (b) (4) (b) (4) FDA recommended Abeona use a more specific (b) (4) that can confirm the presence of their desired cell population in the DP (e.g., keratinocytes), or conduct an additional study to demonstrate that the (b) (4) is specific enough so that only the desired cell population is detected. FDA recommended Abeona add sensitivity to their proposed validation plans for the identity assay.

Abeona also provided a brief overview of the remaining (b) (4) stability data that will be provided, with final reports expected by the end of June 2024. Regarding the proposed (b) (4) stability plan, FDA recommended that the (b) (4) should be (b) (4) instead of the proposed (b) (4) as the acceptable range for (b) (4) is (b) (4) and (b) (4) stability studies should be performed with the worst-case scenario.

2. Discussion of Minor Review Issues

- a. Device design control processes and procedures for PZ combination product were established after the submission of the BLA but have not been submitted as an amendment to the BLA. Additionally, the design validation per Phase II and design completion per Phase III should also be submitted to the BLA once completed.

Meeting Discussion:

FDA acknowledged the information Abeona submitted for the design controls in response to CMC IR #4 (received March 19, 2024). FDA will review and follow up with Abeona if there are any further questions.

3. Additional Applicant Data

Please refer to Meeting Discussion in 1 and 2

4. Information Requests

- a. CMC IR#11 (2/16/24) – Requested data from (b) (4) drug substance (DS) (b) (4) and (b) (4) studies. Expected by the end of March 2024.

Meeting Discussion:

FDA is reviewing the protocol Abeona submitted as part of CMC IR #12. Abeona clarified that the expected final study reports are expected by end of June 2024.

5. Discussion of Upcoming Advisory Committee Meeting

- a. An Advisory Committee meeting is not planned.

Meeting Discussion:

No discussion during the meeting.

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

- a. There is no anticipation of a REMS at this time.

Meeting Discussion:

No discussion during the meeting.

7. Postmarketing Requirements/Postmarketing Commitments

- a. PMR/PMC review is currently ongoing.

Meeting Discussion:

Abeona stated they are open to discuss any potential PMRs or PMCs.

8. Major Labeling Issues

- a. Labeling review is ongoing.

Meeting Discussion:

No discussion during the meeting.

9. Review Plans

- a. Review of the BLA is on-going. We will continue sending IRs as necessary to get clarification on any submitted information. FDA plans to send the labeling comments by April 25, 2024.

Meeting Discussion:

No discussion during the meeting.

10. Applicant Questions

Meeting Discussion:

Please refer to discussions 1 and 2.

11. Wrap-up and Action Items

- a. The Late Cycle Meeting Summary will be sent by April 20, 2024.

Meeting Discussion:

Abeona summarized the action items from the meeting, as described in the substantive review issues discussion above and described in Abeona's LCM presentation.

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.