

Our STN: BL 125613/0

LATE CYCLE MEETING SUMMARY

July 5, 2017

Kamada Ltd.
Attention: Ms. Holli S. Vaughan
Biologics Consulting Group, Inc.
400 North Washington Street, Suite 100
Alexandria, VA 22314

Dear Ms. Vaughan:

Attached is a copy of the memorandum summarizing your June 8, 2017, 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.

If you have any questions, please contact Dr. Jiahua Qian at (240) 402-8432.

Sincerely,

Basil Golding, MD
Director
Division of Plasma Protein Therapeutics
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

ENCLOSURE:
Late-Cycle Meeting Summary
Kamada's material submitted prior to the Late-Cycle Meeting

Late-Cycle Meeting Summary

Meeting Date: June 8, 2017
Meeting Location: 10903 New Hampshire Avenue
WO Bldg 71 – Rm 1208/1210
Silver Spring, MD 20993

Application number: STN BL 125613/0
Applicant: Kamada Ltd
Product name: Rabies Immune Globulin (Human) KEDRAB
Proposed Indication: Passive, transient post-exposure prophylaxis of rabies infection, when given immediately after contact with a rabid or possibly rabid animal and in combination with rabies vaccine

Meeting Chair: Michael Kennedy, PhD
Meeting Recorder: Jiahua Qian, PhD

FDA ATTENDEES

Alfred Del Grosso, PhD, OCBQ/DBSQC
Alpita Popal, PharmD, OCBQ/DCM/APLB
Alvendi Firoozaeh, MD, OBE/DE
Pankaj Amin, OCBQ/DMPQ
Basil Golding, MD, OTAT/DPPT
Becky Robinson-Zeigler, PhD, OTAT/DCEPT/PTB2
Bruce S. Schneider, MD, OTAT/DCEPT
David Menschik, MD, OBE/DE
Dorothy Scott, MD, OTAT/DPPT
Erin McDowell, OCBQ/BM
Ewa Marszal, PhD, OTAT/DPPT
Ilan Irony, MD, OCBQ/DCEPT
Jiahua Qian PhD, OTAT/DRPM
Kimberly Benton, PhD, OTAT
Laurie Norwood, OCBQ/DMPQ
Leslyn Aaron, PhD, OCBQ/DBSQC
Lokesh Bhattacharyya, PhD, OCBQ/DBSQC
Lu Deng, PhD, OTAT/DPPT
Mahmood Farshid, PhD, OTAT/DPPT
Malgorzata Norton, MS, OTAT/DPPT
Michael Kennedy, PhD, OTAT/DPPT
Micheal Ovanesov PhD, OTAT/DPPT
Olga Simakova, PhD, OTAT/DPPT
Shuya Lu, PhD, OBE/DB
Tejashri Purohit-Sheth, MD, OTAT/DCEPT
Varsha Garnepudi, MS, OCBQ/DBSQC
Wilson Bryan, MD, OTAT
Xiaofei Wang, PhD, OTAT/DCEPT
Hsiaoling Wang, PhD, OCBQ/DBSQC

Kamada ATTENDEES

Orit Pinchuk, MSc
Naveh Tov, MD

Alma Levy
Liliana Bar, PhD
Yuval Sagiv
Hanna Ash
Roberto Meidler
Galit Afik
Wang, Yu-Fen

Garrett Bergman, MD, MBA
Ruth Ellis, MD, MPH
Holli S. Vaughan, MS, RAC

Vice President Regulatory Affairs, Kamada Ltd.
Vice President Medical Affairs & Clinical
Development, Kamada
Regulatory Affairs Director, Kamada Ltd.
Vice President, Research and Development
R&D Director
R&D Director
R&D Director
QA Director, Production plant
Head of US Regulatory Affairs, Kedrion BioPharma,
Inc.
Sr. Director, Medical Affairs, Kedrion BioPharma, Inc.
Sr. Clinical Consultant, Biologics Consulting
Associate, Biologics Consulting

BACKGROUND

BLA STN BL 125613/0 was submitted on August 29, 2016, for Rabies Immune Globulin (Human) [KEDRAB]

Proposed indications: Passive, transient post-exposure prophylaxis of rabies infection, when given immediately after contact with a rabid or possibly rabid animal and in combination with rabies vaccine

PDUFA goal date: August 29, 2017

In preparation for this meeting, FDA issued the Late-cycle Meeting Material on May 24 , 2017.

DISCUSSION:

Introductory Comments:

FDA welcomed Kamada and outlined the discussion for the meeting.

FDA stated that the meeting is not intended to discuss the pending regulatory decision on the application, but a forum to provide an update on the review and clarifications to the meeting material sent on May 24, 2017 and recent information requests.

1. Discipline Review Letters

No Discipline Review letters have been issued to date.

2. Substantive Review Issues discussed during the LCM

For inspections: Inspections are complete. The agency expected Kamada to provide the time line for completion of the proposed (b) (4) media fill studies. As (b) (4) will be used including the aseptic filling of the HRIG product, we recommend completion of the proposed media fill studies at least 30 days before the BL 125613/0 action due date (8/29/2017).

Prior to the LCM, Kamada provided information to address the media fill study. The media fill lots were repeated for the failed configuration ((b) (4)). The data is summarized in the attached document and will be included as part of the meeting summary.

FDA said that the information provided by Kamada is acceptable.

3. Questions from FDA information request discussed during the LCM

Kamada's Questions to CMC Information Request, dated May 31, 2017.

1. Kamada would like to get clarification on the FDA claim: " The (b) (4) robustness studies were performed with material not representative of the in-process material, and therefore, do not adequately validate the broad operating parameters."

FDA mentioned that the in-process material used for the (b) (4) studies was not handled the same way as it would be during routine manufacturing. For example, the material used for the (b) (4) robustness contained (b) (4), which is not used during the routine manufacturing process. Kamada replied that they tested the material and found it was equivalent. FDA asked Kamada to provide data to show equivalence of the in-process material used in the robustness studies to routine manufacturing material. FDA will review the data and respond to Kamada.

2. Kamada would like to discuss with FDA their request "please perform a full scale process validation on (b) (4) new conformance lots. (b) (4) of each range of critical process parameters and (b) (4)." ."

FDA asked Kamada to provide a response to the IR questions, which include a request for data to support the manufacturing ranges. FDA will make a decision and respond to Kamada regarding this issue once the data are reviewed.

Kamada's Questions to DBSQC Information Request

3. Kamada would like to discuss FDA's (b) (4) and Kamada's revised method (b) (4), specifically:

- The difference in separation capability of the two methods; FDA's and Kamada's revised method ((b) (4)) specifically related to (b) (4).
- Does FDA method implement two (b) (4) practice?
- To understand FDA's approach for preferred method.

FDA stated that the sponsor has the option to either adopt CBER's published method to determine the (b) (4), which shows better separation of the peaks, or use their proposed method. If the sponsor chooses the former, the method needs a complete validation with (b) (4) DP samples of this product. If the sponsor chooses the latter, the method needs to be validated for accuracy, precision, linearity, range and limit of quantitation (LOQ) for the (b) (4). In either case, the sponsor needs to set a specification for (b) (4). In addition, the method of (b) (4), especially of (b) (4) that are not (b) (4), needs to be decided and justified based on the (b) (4) and resolution of the (b) (4). It is important that the same approach is used consistently for all samples.

4. FDA sent the following clinical information request to Kamada and asked a clarification.
- You stated that there were 1863 cases of individuals exposed to a rabid animal during 2010-2015. You also stated that 1863 individuals were confirmed to have been exposed to a rabid animal and received PEP with KamRAB. During this period there were no reports of illness or death due to rabies, and no reports of serious adverse events related to the administration of KamRAB. Were the 1863 subjects actively followed to ensure that they did not develop rabies or was it by inference that none of them contracted rabies?

Kamada stated that health records are managed by Israel Health Ministry and they will try to get more information from the Israeli authorities.

3. Advisory Committee (AC) Meeting

AC Meeting is not planned.

4. Risk Management Actions (e.g., REMS)

REMS is not required

5. Summary and Action Items

FDA said that there was difficulty in hearing the Kamada representatives during the call, and asked Kamada to provide a summary on what they said during the meeting. FDA and Kamada agreed to continue communications through information requests.

6. Post-Meeting Comments

PMC was not discussed at LCM.

End