Our STN: BL 12566100

LATE-CYCLE MEETING MEMORANDUM
June 14, 2018

Bayer Healthcare, Inc.
Attention: Michelle Meng, PhD
100 Bayer Boulevard
Whippany, NJ 07981

Dear Dr. Meng:

Attached is a copy of the memorandum summarizing your May 29, 2018 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 Candace Jarvis at (240) 402-8315.

Sincerely,

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

Late-Cycle Meeting Summary

Meeting Date and Time:	May 29, 2018, 1:00PM-2:00PM
Meeting Location:	Teleconference
Application Number:	125661/0
Product Name:	Antihemophilic Factor (Recombinant), PEGylated
Proposed Indications:	For controlling and preventing bleeding episodes and for surgical and long term prophylaxis in patients with hemophilia A
Applicant Name:	Bayer Healthcare, Inc
Meeting Chair:	Zuben Sauna, PhD
Meeting Recorder:	Candace Jarvis Kay Owosela

FDA ATTENDEES

Ritu Agarwal, PhD, CBER/OCBQ/DSQBC
Kimberly Benton, PhD, CBER/OTAT
Najat Bouchkouj, MD, CBER/OTAT/DCEPT
Susanne Carter
Graca Dores, MD, MPH, CBER/OBE/DE/AEB
Parmesh Dutt, PhD, CBER/OCBQ/DSQBC
Maryna Eichelberger, PhD, CBER/OCBQ/DBSQC
Varsha Garnepudi, PhD, CBER/OCBQ/DSQBC
Bindu George, MD, CBER/OTAT/DCEPT
Lin Huo, PhD, CBER/OTAT/OBE
Candace Jarvis, CBER/OTAT/DRPM
Bhanu Kannan, MS, CBER
Daniel Lagasse, PhD, CBER/OTAT/DPPT
Timothy Lee, PhD, CBER/OTAT/DPPT
Iftekhar Mahmood, PhD, CBER/OTAT/DCEPT
Rob McElwain
Olukayode Owosela, MSc, CBER/OTAT/DRPM
Ze Peng, PhD, CBER/OTAT/DPPT
Tejashri Purohit-Sheth, MD, CBER/OTAT/DCEPT
Renee Rees, PhD, CBER/OBE
Sandhya Sanduja, PhD, CBER/OTAT/DCEPT

APPLICANT ATTENDEES

Olubunmi Afonja, MD, US Medical Affairs
Andreas Baumann, PhD, DMPK
Jim Cassaday, Data Management
Monika Maas Enriquez, MD, Clinical
Alex Frumin, Data Management
Matthias Hoepfner, PhD, Regulatory CMC
Inge Ivens, PhD, Toxicology
Yvonne Katterle, PhD, Bioanalytics

Joel Krasnow, MD, Pharmacovigilance
Chi Li, PhD, Regulatory
Michelle Meng, PhD, Regulatory
Lisa Michaels, MD, Clinical
Todd Paporello, PharmD, Regulatory
Susan Radke, Clinical Project Management
Lisa Regan, PhD, CMC
Kapil Saxena, MD, Clinical
Silvana Schumacher-Goethel, PhD, Regulatory
Anita Shah, PhD, Clinical Pharmacology
John Teare, PhD, CMC
Despina Tseneklidou-Stoeter, Clinical project management
Rene Walsch, PhD, Study Management
Maria Wang, Statistics
Megan Ward, Regulatory CMC

BACKGROUND

BLA 125661/0 was submitted on August 30, 2017, for Antihemophilic Factor (Recombinant), PEGylated.

Proposed indication: For controlling and preventing bleeding episodes and for surgical and long term prophylaxis in patients with hemophilia A

PDUFA goal date: August 30, 2018

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on May 22, 2018.

DISCUSSION

1. Discussion of Substantive Review Issues -00 minutes

   There are no substantive issues to date

2. Discussion of Minor Review Issues – 00 minutes

   There are no minor review issues to date

3. Additional Applicant Data –00 minutes

   There were no additional applicant data submitted.

4. Information Requests (IR)-05 minutes

   a. FDA acknowledged amendment 37 (serial# 38) dated and received on May 15, 2018 regarding commitments made to provide results from validation studies to address IR #24/question 2 and IR #25/question 1.
   b. FDA acknowledged amendment 38 (serial# 39) dated and received on May 16, 2018 regarding the process by which upload failures from subject diaries were addressed to provide efficacy analysis data.
   c. FDA acknowleged amendment 39 (serial # 40) dated and received on May 22, 2018 regarding commitments made to provide results from validation studies to address IR#27 question 3a.
   d. FDA acknowledged amendment 40 (serial# 41) dated and received on May 23, 2018 regarding the interim audited study report for the study titled, 'A 13- and 26-Week Intravenous Toxicity Study of BAY 94-9027 in the Nude Rat (b) (4) nude rats,(b) (4)) followed by a 26-Week Recovery Period'.
   e. FDA acknowleged amendment 41 (serial# 42) dated and received on May 23, 2018 regarding details of the efficacy analysis and data sets of subjects treated in study 13024.

5. Discussion of Upcoming Advisory Committee Meeting – 00 minutes

   There was no discussion of an upcoming Advisory Committee Meeting

6. Risk Management Actions (e.g., REMS) – 00 minutes

   There was no discussion of risk management actions as it is not applicable.

7. Postmarketing Requirements/Postmarketing Commitments – 10 minutes

   a. Dependent on findings from the Pharmacology/Toxicology review of the submitted data.

   b. The current PVP includes assessments related to the PROTECT KIDs study (individuals <12 years of age). These PVP elements are included in the sections on "important identified risks" (development of FVIII inhibitors, hypersensitivity, lack of drug effect) and "missing information" (potential long-term PEG-related adverse reactions). Please remove "PROTECT KIDs" elements from the PVP since this study is being conducted in individuals outside the age range for which product approval is being sought. The PROTECT KIDs study will

need to be monitored through another mechanism (i.e., IND) Please note that currently planned questionnaires may become obsolete or may need to be added pending the Pharmacology/Toxicology review. An IR may be sent once required questionnaires are decided upon.

c. Bayer proposed PMC (b) (4) assay

Additonal Discussion: The sponsor agreed to update PVP to remove statement of treating children <12 years of age. FDA reiterated that based upon the Pharmacology/ Toxicology findings, questionnaire(s) may not be needed or new questionnaire(s) may need to be added. FDA also stated that the data based upon receipt of the current responses submitted in amendment 34 that data looks fine and as of now there will be no PMC commitments.

8. Major Labeling Issues – 00 minutes

   There are no labeling issues at this time.

9. Review Plans – 01 minutes

   Additonal Discussion: The Pharmacology/Toxicology review is still ongoing. The BLA review disciplines have no outstanding issues to report at this time and the review team is on-target for the proposed action due date.

10. Applicant Questions- 05 minutes

    Additonal Discussion: The sponsor confirmed that they were on-track in submitting the validation supplement regarding NaCL method using Damoctocog Alfa Pegol by May 3oth. There was also discussion of additional realtime stability data to further support their proposed shelf life and storage conditions.

11. Wrap-up and Action Items – 02 minutes

    Action Item: The sponsor plans to update their PVP to remove children <12 years of age.

This application is currently still under review; therefore, this meeting did not address the final regulatory decision for the application.