CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761355Orig1s000

OTHER ACTION LETTERS

BLA 761355

COMPLETE RESPONSE

Regeneron Pharmaceuticals, Inc.
Attention: Donato Forlenza, PharmD, MBa
Senior Director, Regulatory Affairs
777 Old Saw Mill River Road
Tarrytown, NY 10591

Dear Dr. Forlenza:

Please refer to your biologics license application (BLA) dated and received December 27, 2022, and your amendments, submitted under section 351(a) of the Public Health Service Act for Eylea HD (aflibercept) Injection. We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product do not comply with the current good manufacturing practice regulations in parts 210 and 211. FDA conveyed deficiencies to the representative of the drug product manufacturing facility listed in this application following a pre-license inspection of the (b) (4) , facility. Satisfactory resolution of the observations is required before this BLA submission may be approved.

PROPRIETARY NAME

Please refer to correspondence dated, March 27, 2023, which addresses the proposed proprietary name, Eylea HD. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiency.

SAFETY UPDATE

When you respond to the above deficiency, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the product under consideration regardless of indication, dosage form, or dose level.

ADDITIONAL COMMENTS

We have the following comment/recommendation that is not an approvability issue:

Please perform real-world shipping studies, covering worst case shipping conditions (i.e., routes and modes of transportation, distance, duration, temperature, packing configuration, and shipping containers employed) on the final drug product (DP) in the proposed container closure system to ensure there

is no impact to product quality and sterility of the DP (i.e., comparison of pre-shipment to post-shipment data, assessed against pre-defined acceptance criteria).

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 601.3(b)). If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 601.3(c). You may also request an extension of time in which to resubmit the application.

A resubmission must fully address the deficiency listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiency outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The product may not be legally marketed until you have been notified in writing that this application is approved. If you have any questions, please contact Michael Puglisi, Regulatory Project Manager, at michael.puglisi@fda.hhs.gov or at (301) 796-0791.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Director
Division of Ophthalmology
Office of Specialty Medicine
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

WILEY A CHAMBERS
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