CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761365Orig1s000

OTHER ACTION LETTERS

BLA 761365

COMPLETE RESPONSE

Astellas Pharma US, Inc.
Attention: Sarah Groenendal, M.S., RAC
Associate Director, Regulatory Affairs
Astellas Pharma Global Development, Inc.
2375 Waterview Drive
Northbrook, IL 60062

Dear Sarah Groenendal:

Please refer to your biologics license application (BLA) dated May 12, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for IMAB362.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

Following the pre-license inspection of (b) (4) listed in this application, FDA conveyed deficiencies to the facility's representative. FDA has reviewed the facility's responses to the referenced deficiencies, and all deficiencies have not been satisfactorily resolved. Satisfactory responses to these deficiencies should be provided to the inspection team prior to submitting your complete response. Your complete response should include the date of the facility's response to the FDA Form 483. The assessment of application approvability and the resolution of inspection deficiencies would be evaluated upon receipt of the complete response and may include re-inspection of the facility. Please work with the facility in resolving the related deficiencies.

ADDITIONAL COMMENTS

We have the following comments/recommendations that are not approvability issues:

1. The description of the sterility test method for IMAB362 drug product release indicates the total volume tested for each medium is 10 reconstituted vials, however sterility testing should test 20 vials for each medium and half the contents of each container in accordance with USP <71>. Clarify whether the sterility method is

performed according to the USP <71> compendial method and update the method procedure in section 3.2.P.5.2 accordingly.

2. The container closure integrity test (CCIT) method used for drug product stability testing was validated for specificity and detection limit (refer to Table 2 of section 3.2.P.8.3). However, the CCIT method is non-compendial and should also be validated for precision (repeatability, intermediate precision, and reproducibility) and robustness (capacity of method to remain unaffected by deliberate variations in method parameters). Provide complete CCIT method validation results for the proposed dye ingress method. Refer to FDA Guidance for Industry: Analytical Procedures and Methods Validation for Drugs and Biologics, 2015.

3. You plan (b) (4) for commercial manufacture of IMAB362 drug product. You evaluated (b) (4) (b) (4) Provide additional data and/or information to support that the (b) (4) is capable of manufacturing IMAB362 drug product reproducibly.

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

CARTON AND CONTAINER LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to correspondence dated, March 23, 2023, which addresses the proposed proprietary name, VYLOY. This name was found conditionally acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to all of the application deficiencies that have been identified in this letter.

[1] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources
[2] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule

SAFETY UPDATE

When you respond to the above deficiencies, 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 drug under consideration regardless of indication, dosage form, or dose level.

a. Describe in detail any significant changes or findings in the safety profile.

b. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
- Present tabulations of the new safety data combined with the original application data.
- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.
- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

c. Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

d. Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.

e. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.

f. Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

g. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

h. Provide English translations of current approved foreign labeling not previously submitted.

OTHER

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 all the deficiencies 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 deficiencies 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, call Nataliya Fesenko, Pharm.D., Senior Regulatory Health Project Manager, at (240) 402-6376.

Sincerely,

{See appended electronic signature page}

Paul G. Kluetz, M.D.
Supervisory Associate Director (Acting)
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation & 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/

PAUL G KLUETZ
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