

NDA 215833/S-021  
NDA 215833/S-024

## **SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals Corporation  
Attention: Lisa Daniel  
Senior Global Program Regulatory Manager  
One Health Plaza, USEH\_337-A22  
East Hanover, NJ 07936

Dear Lisa Daniel:

Please refer to your supplemental new drug applications (sNDAs) dated June 28, 2024 (S-021) and October 21, 2024 (S-024), received June 28, 2024 and October 21, 2024, respectively, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pluvicto (lutetium Lu 177 vipivotide tetraxetan).

These Prior Approval sNDAs provide for the following:

- S-021: Revising the indication to treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy, and are considered appropriate to delay taxane-based chemotherapy, or have received prior taxane-based chemotherapy, based on the results of study CAAA617B12302 (PSMAfore).
- S-024: Revising the US Prescribing Information based on the final clinical study report for study CAAA617A12301 (PSMA-617-01; VISION), which adds new adverse drug reactions and preferred terms.

### **APPROVAL & LABELING**

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (Prescribing Information), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(I)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for S-021 because necessary studies are impossible or highly impracticable due to indication of prostate cancer.

Because none of these criteria apply to S-024, you are exempt from this requirement for that application.

### **POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitment.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

**For NDA 215833/S-021:**

- 4824-1 Conduct an image-based dosimetry study calculating the radiation absorbed dose to the bone marrow resulting from treatment with <sup>177</sup>Lu-PSMA-617, using the scans collected from the VISION sub-study; considering all the activity in the organs, tissues, and lesions; and following the methodology discussed with the FDA. Provide the average value for all patients and for subgroups of patients with high and low disease burden in bone including categories of unaffected and affected red marrow based on vertebra with no isolated lesions and extensive lesion activity. Also calculate the absorbed dose to the osteogenic cells.

The timetable you submitted on March 18, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	04/2025
Final Protocol Submission:	06/2025
Study Completion:	08/2025
Final Report Submission:	09/2025

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 133661 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>3</sup>

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at [FDA.gov](http://FDA.gov).<sup>4</sup> Information and Instructions for completing the form can be found at [FDA.gov](http://FDA.gov).<sup>5</sup>

### **PATENT LISTING REQUIREMENTS**

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Alice Lee, Senior Regulatory Project Manager, at (301) 796-8881 or at [Alice.Lee@fda.hhs.gov](mailto:Alice.Lee@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Daniel Suzman, MD  
Deputy Director  
Division of Oncology 1  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

### **ENCLOSURES:**

- Content of Labeling
  - Prescribing Information

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<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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**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.**  
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/s/  
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DANIEL L SUZMAN  
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