NDA 218033/S-002
NDA 218033/S-003

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENT/COMMITMENT**

Day One Biopharmaceuticals, Inc.
Attention: Cydrienne Chatto, BS
Director, Regulatory Science
1800 Sierra Point Parkway, Suite 200
Brisbane, CA 94005

Dear Cydrienne Chatto:

Please refer to your supplemental new drug applications (sNDA) dated and received March 3, 2025 (S-002) and March 31, 2025 (S-003), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ojemda (tovarafenib) for oral suspension.

Prior Approval sNDA 002 provides for updates to the U.S. Prescribing Information (USPI) and Patient Information labeling, based on safety and efficacy data generated from Study DAY101-001/PNOC026 (FIREFLY-1); references the availability of an FDA-approved companion diagnostic; and provides for minor updates to the Instructions For Use labeling.

Prior Approval sNDA 003 provides for updates to the USPI labeling, based on data from a carcinogenicity study entitled “A 26-Week Carcinogenicity Study of DAY101 by Oral Gavage Administration in Hemizygous CByB6F1-Tg(HRAS)2Jic Mice,” to fulfill postmarketing requirement 4626-2.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, Instructions for Use), with the addition of any labeling changes in pending "Changes Being Effected" (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*.[2]

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(l)(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.

Because none of these criteria apply to your supplemental applications, you are exempt from this requirement.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] 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.

FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENT

We have received your submissions dated July 12, 2024, and March 31, 2025, reporting on the following postmarketing requirement/commitment listed in the April 23, 2024, approval letter.

4626-2 Conduct a carcinogenicity study in mice to evaluate the potential serious risk of carcinogenicity.

4626-11 Conduct an appropriate analytical and clinical validation study to support the development of an in vitro diagnostic device using clinical trial data that demonstrates that the device is essential to the safe and effective use of tovorafenib for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation.

We have reviewed your submissions and conclude that the above requirement/commitment were fulfilled.

We remind you that there are postmarketing requirements and postmarketing commitments listed in the April 23, 2024, approval letter that are still open.

We remind you that accelerated approval PMR 4626-1 listed in the April 23, 2024, approval letter is still open. Pursuant to 21 CFR 314.510 (Subpart H), continued approval of the drug is contingent upon verification and description of clinical benefit and completion of the clinical trial for PMR 4626-1.

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.*[3]

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.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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 Opeyemi Udoka, Senior Regulatory Health Project Manager, at 240-402-4558 or Opeyemi.Udoka@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Nicole Drezner, M.D.
Deputy Director
Division of Oncology 2
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use

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/

NICOLE L DREZNER
08/27/2025 01:10:00 PM