NDA 219304

NDA APPROVAL

Deciphera Pharmaceuticals, LLC
Attention: Priyanka Kamath, MS, RAC
Director, Regulatory Affairs
200 Smith Street
Waltham, MA 02451

Dear Priyanka Kamath:

Please refer to your new drug application (NDA) dated and received June 17, 2024, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Romvimza (vimsetinib) capsules.

This NDA provides for the use of Romvimza (vimsetinib) capsules for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) for which surgical resection will potentially cause worsening functional limitation or severe morbidity.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is 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 and Medication Guide) 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 via publicly available labeling repositories.

[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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, and to the carton and container labeling submitted on February 10, 2025 as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 219304**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Romvimza (vimsetinib) capsules shall be 24 months from the date of manufacture when stored at 20–25° C.

ADVISORY COMMITTEE

Your application for Romvimza was not referred to an FDA advisory committee because the application did not raise significant public health questions regarding the role of vimseltinib for patients with symptomatic TGCT that would benefit from an external committee of experts.

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 this application because necessary studies are impossible or highly impracticable to conduct in the pediatric population given the extreme rarity of TGCT in patients <17 years of age.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an

unexpected serious risk of carcinogenicity and to assess a signal of serious risk of hepatotoxicity.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4791-1 Complete the ongoing 104-week rat carcinogenicity study (Study No. DCC-3014-04-0025) to evaluate the potential for carcinogenicity.

The timetable you submitted on February 5, 2025, states that you will conduct this study according to the following schedule:

Study Completion:	05/2025
Final Report Submission:	06/2025

4791-2 Conduct a prospective clinical registry to evaluate the potential risk of serious hepatotoxicity in patients receiving vimseltinib for the treatment of tenosynovial giant cell tumor. Analyses should include evaluation of alanine aminotransferase, aspartate aminotransferase, bilirubin, symptoms suggestive of hepatotoxicity, and dose reduction and treatment discontinuation related to hepatotoxicity. Include investigations of time to event and severity, and potential risk factors such as age, race, and comorbidities. The registry should aim to enroll at least 100 patients. Monitor patients until discontinuation of study treatment or a minimum of 5 years from start of treatment, whichever occurs first. Interim safety analyses should be performed yearly beginning one year after the first patient has received vimseltinib to characterize the long-term risk of hepatotoxicity with vimseltinib.

The timetable you submitted on February 5, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	06/2025
Final Protocol Submission:	10/2025
Interim Report Submission #1:	05/2026
Interim Report Submission #2:	05/2027
Interim Report Submission #3:	05/2028
Interim Report Submission #4:	05/2029
Interim Report Submission #5:	05/2030
Study Completion:	12/2030
Final Report Submission:	05/2031

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess a signal of serious risk of increased drug toxicity in patients with moderate hepatic impairment and when vimseltinib is used concomitantly with sensitive BCRP, OATP1B1, OATP1B3, and OCT2 substrates.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following trials:

4791-3 Conduct a clinical pharmacokinetic trial to evaluate the serious potential risk of increased drug toxicity and determine an appropriate dose of vimseltinib to minimize potential serious toxicity, in patients with moderate hepatic impairment using the NCI-ODWG criteria. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled "Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling."

The timetable you submitted on February 5, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	03/2025
Final Protocol Submission:	07/2025
Trial Completion:	07/2026
Final Report Submission:	02/2027

4791-4 Conduct a clinical pharmacokinetic trial to evaluate the effect of multiple doses of vimseltinib on the single dose pharmacokinetics of a sensitive BCRP substrate to evaluate the serious potential risk of increased drug toxicity. Design and conduct the trial in accordance with the ICH Harmonized Guidance entitled "M12 Drug Interaction Studies."

The timetable you submitted on February 5, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	04/2025
Final Protocol Submission:	08/2025
Trial Completion:	06/2026
Final Report Submission:	12/2026

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm

4791-5 Conduct a clinical pharmacokinetic trial to evaluate the effect of multiple doses of vimseltinib on the single dose pharmacokinetics of sensitive OATP1B1 and OATP1B3 substrates to evaluate the serious potential risk of increased drug toxicity. Design and conduct the trial in accordance with the ICH Harmonized Guidance entitled "M12 Drug Interaction Studies."

The timetable you submitted on February 5, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission: 04/2025
Final Protocol Submission: 08/2025
Trial Completion: 06/2026
Final Report Submission: 12/2026

4791-6 Conduct a clinical pharmacokinetic trial to evaluate the effect of multiple doses of vimseltinib on the single dose pharmacokinetics of a sensitive OCT2 substrate to evaluate the serious potential risk of increased drug toxicity. Design and conduct the trial in accordance with the ICH Harmonized Guidance entitled "M12 Drug Interaction Studies."

The timetable you submitted on February 5, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission: 04/2025
Final Protocol Submission: 08/2025
Trial Completion: 06/2026
Final Report Submission: 12/2026

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Submit clinical protocol(s) to your IND 131218 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o), REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).**

[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

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.*[5]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

REPORTING REQUIREMENTS

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

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

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We request that for Romvimza, you submit all cases describing serious adverse reactions related to hepatotoxicity as 15-day "Alert reports" (described under 21 CFR 314.80(c)(1)) through the 3rd year following initial U.S. approval, for patients whose data is not captured in the registry.

We request that you provide a separate narrative summary and analysis for cases that are identified as serious cases of hepatotoxicity, involving Romvimza, in each required postmarketing periodic safety report (e.g., Periodic Adverse Drug Experience Report [PADER] required under 21 CFR 314.80(c)(2)), for patients whose data is not captured in the registry.

Your narrative summary and analysis should include an interval and cumulative assessment of each event and a line listing of the cases for the reporting interval. Your narrative summary should include an assessment of the following:

- Description of any event of serious hepatotoxicity involving Romvimza, including but not limited to laboratory values and clinical status of the patient, concomitant medications, and timing of event in relation to vimseltinib dosing.

- Action taken in response to an event of serious hepatotoxicity involving Romvimza, including but not limited to hospitalization status, treatments administered, and supportive care.

- Outcome of an event of serious hepatotoxicity involving Romvimza.

- Outcome of retreatment after an event of serious hepatotoxicity involving Romvimza, if applicable.

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share

application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website[8].

If you have any questions, call Haroon Vohra, Pharm.D., Senior Regulatory Project Manager, at 240-402-4471.

Sincerely,

{See appended electronic signature page}

Paul Kluetz, MD
Supervisory Associate Director for Solid Tumor Oncology (Acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

[8] https://www.uspnf.com/

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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