NDA 220425

NDA APPROVAL

Elevar Therapeutics Inc.
Attention: Young-Sil (Anna) Yim
Executive Director, Regulatory Affairs
1 Bridge Plaza North, Suite 850
Fort Lee, NJ 07024

Dear Young-Sil (Anna) Yim:

Please refer to your new drug application (NDA) received January 27, 2026, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Lyrfigtu (lirafugratinib) capsule.

This NDA provides for the use of Lyrfigtu (lirafugratinib) capsule for the treatment of adults with previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma harboring a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement.

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 Patient Package Insert) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in 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 carton and container labeling submitted on September 18, 2026, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to 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 220425**." 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 Lyrfigtu (lirafugratinib) capsule shall be 36 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

ADVISORY COMMITTEE

Your application for Lyrfigtu was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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 studies requirement for this application, in pediatric patients less than 17 years of age because necessary studies are impossible or highly impracticable, due to the exceedingly low incidence of FGFR2 altered tumors.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FD&C Act 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 FD&C Act will not be sufficient to assess

known serious risks of severe stomatitis, palmar-plantar erythrodysesthesia syndrome, retinal pigment epithelial detachment, and nail toxicities; and to assess a signal of a serious risk of increased drug toxicity when lirafugratinib is used concomitantly with sensitive P-gp and BCRP substrates.

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

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess these serious risks.

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

5057-1 Conduct a randomized clinical trial to further characterize known serious risks with lirafugratinib including severe stomatitis, palmar-plantar erythrodysesthesia syndrome, retinal pigment epithelial detachment, and nail toxicities, and to compare the safety and activity of lirafugratinib 70 mg once daily versus a lower dosage in patients with previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma harboring FGFR2 fusions or other rearrangements, who have not received prior FGFR inhibitors.

The timetable you submitted on September 1, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	01/2027
Final Protocol Submission:	05/2027
Trial Completion:	11/2031
Final Report Submission:	05/2032

5057-2 Conduct a clinical pharmacokinetic trial to assess a serious potential risk of increased drug toxicity by evaluating the effect of repeat doses of lirafugratinib on the single dose pharmacokinetics of a sensitive P-gp and BCRP substrate and inform appropriate management strategies for clinically relevant drug interactions. Design and conduct the trial in

accordance with the ICH Harmonized Guidance for Industry entitled “M12 Drug Interaction Studies.”

The timetable you submitted on September 1, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	01/2027
Final Protocol Submission:	05/2027
Trial Completion:	05/2032
Final Report Submission:	09/2032

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]

Submit clinical protocol(s) to your IND 147405 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).**

Section 505(o)(3)(E)(ii) of the FD&C Act 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 FD&C Act, 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 FD&C Act section 505(o)(3)(E)(ii) and could result in enforcement action.

[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.

POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

5057-3 Conduct adequate analytical and clinical validation studies to support revisions to the labeling of lirafugratinib to specify the use of an FDA-authorized in vitro companion diagnostic device to accurately and reliably identify patients using blood and/or tissue samples who have FGFR2 fusions and other rearrangements and for whom lirafugratinib therapy is indicated.

The timetable you submitted on September 1, 2026, states that you will conduct this study according to the following schedule:

Study Completion:	01/2029
Final Report Submission:	09/2029

The final study report should be accompanied by a labeling supplement to incorporate information about the use of an FDA-authorized companion diagnostic device.

Submit clinical protocols to your IND 147405 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 guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*

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

REPORTING REQUIREMENTS

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

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[6].

If you have any questions, contact Rebecca Cohen, Regulatory Health Project Manager, at Rebecca.cohen@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Laleh Amiri-Kordestani, MD
Acting Deputy Director
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[6] https://www.uspnf.com/

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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/

LALEH AMIRI KORDESTANI
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