NDA 220359

ACCELERATED APPROVAL

AstraZeneca Pharmaceuticals LP
Attention: Ping Hu, PhD
Regulatory Affairs Director
1 Medimmune Way
Gaithersburg, MD 20878

Dear Dr. Hu:

Please refer to your new drug application (NDA) dated May 27, 2025, received May 27, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Etcamah (camizestrant) tablets.

We acknowledge receipt of your major amendment dated February 27, 2026, which extended the goal date by three months.

This NDA provides for the use of Etcamah (camizestrant) tablets in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy, based on an FDA-authorized test.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved under accelerated approval pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and 21 CFR 314.510, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the accelerated approval statutory provisions and regulations.

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 text for the Patient Package Insert). 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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, 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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 220359**." 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 Etcamah (camizestrant) tablets shall be 36 months from the date of manufacture when stored at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-86°F) [see USP Controlled Room Temperature].

ACCELERATED APPROVAL REQUIREMENTS

Pursuant to section 506(c) of the FDCA and 21 CFR 314.510 you are required to conduct further adequate and well-controlled clinical trials intended to verify and describe clinical benefit. You are required to conduct such clinical trials with due diligence. If required postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, including with respect to the conditions set forth below, we may withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated August 19, 2026. These requirements are listed below.

5047-1 Complete a randomized trial in patients with HR+/HER2- MBC receiving first-line treatment with an aromatase inhibitor and CDK4/6 inhibitor which compares changing therapy to camizestrant with continued CDK4/6 inhibitor at *ESR1*m detection (prior to radiographic progression) to changing therapy to camizestrant +/- continued CDK4/6 inhibitor at radiographic disease progression for verification of the clinical benefit with

[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.

camizestrant and submit the prespecified time to strategy failure (TSF) and overall survival (OS) results.

The timetable you submitted on August 19, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission: 10/2026
Final Protocol Submission: 04/2027
Trial Completion: 03/2032
Final Report Submission: 09/2032

5047-2 Complete the ongoing clinical trial SERENA-6, titled "A Phase 3, Double-blind, Randomized Study to Assess Switching to Camizestrant + CDK4/6 Inhibitor versus Continuing Aromatase Inhibitor (Letrozole or Anastrozole) + CDK4/6 Inhibitor in HR+/HER2- MBC Patients with Detectable ESR1 Mutation Without Disease Progression During 1L Treatment with Aromatase Inhibitor + CDK4/6 Inhibitor – A ctDNA Guided Early Switch Study" to provide the final overall survival results for verification of clinical benefit of camizestrant.

The timetable you submitted on August 19, 2026, states that you will conduct this trial according to the following schedule:

Trial Completion: 09/2028
Final Report Submission: 12/2028

Submit clinical protocols to your IND 151223 for this product. 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.

You must submit status reports of the progress of each clinical trial required under section 506(c) (listed above) to the NDA 180 days after the date of approval of this NDA and approximately every 180 days thereafter (see section 506B(a)(2) of the FDCA) (hereinafter "180-day reports").

You are required to submit two 180-day reports per year for each open study or clinical trial required under section 506(c). The initial report will be a standalone submission and the subsequent report will be combined with your application's annual status report (ASR) required under section 506B(a)(1) of the FDCA and 21 CFR 314.81(b)(2). The standalone 180-day report will be due 180 days after the date of approval (with a 60-day grace period). Submit the subsequent 180-day report with your application's ASR.

Submit both of these 180-day reports each year until the final report for the corresponding study or clinical trial is submitted[3].

Your 180-day reports must include the information listed in 21 CFR 314.81(b)(2)(vii)(a). FDA recommends that you use FORM FDA 3989, *PMR/PMC Annual Status Report for Drugs and Biologics,* to submit your 180-day reports.[4]

180-day reports must be clearly designated "**NDA 220359 180-Day AA PMR Progress Report**."

FDA will consider the submission of your application's ASR under section 506B(a)(1) and 21 CFR 314.81(b)(2), in addition to the submission of reports 180 days after the date of approval each year (subject to a 60-day grace period), to satisfy the periodic reporting requirement under section 506B(a)(2).

Submit final reports to this NDA as a supplemental application. For administrative purposes, the cover page of all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirement(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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric studies requirement for this application because necessary studies are impossible or highly impracticable as breast cancer is rare in the pediatric population.

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 the

[3] You are required to submit information related to your confirmatory trial as part of your annual reporting requirement under section 506B(a)(1) until the FDA notifies you, in writing, that the Agency concurs that the study requirement has been fulfilled or that the study either is no longer feasible or would no longer provide useful information.
[4] FORM FDA 3989, along with instructions for completing this form, is available on the FDA Forms web page at https://www.fda.gov/about-fda/reports-manuals-forms/forms.

known serious risk of QTc interval prolongation, and the signal of the serious risk of increased drug toxicities when camizestrant is coadministered with sensitive substrates of CYP2B6, and transporter substrates of P-gp and BCRP.

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 clinical trials (rather than nonclinical or observational studies) will be sufficient to assess these risks.

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

5047-3 Conduct a pharmacokinetic and pharmacodynamic trial of camizestrant 75 mg and 150 mg once daily for at least 15 days used alone to more fully characterize the effect of camizestrant on the QTc interval. Include adequate baseline heart rate and QTc interval evaluation (e.g., minimum of 48 hours) in all subjects to ensure sufficient pre-dose data to evaluate the post-dose QTc interval effects as measured by the most appropriate heart rate correction method (e.g., individualized (QTcI) and Fridericia (QTcF) QT interval correction methods). Fully capture expected QTC interval effects at peak and trough concentrations of camizestrant.

The timetable you submitted on August 19, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	10/2026
Final Protocol Submission:	12/2026
Trial Completion:	01/2029
Final Report Submission:	07/2029

5047-4 Conduct a clinical drug interaction study to evaluate the effect of camizestrant on the pharmacokinetics of a sensitive substrate of CYP2B6 to assess the magnitude of exposure change of these substrates and serious potential risk of increased drug toxicity, and inform an appropriate drug interaction management strategy for coadministration of camizestrant with CYP2B6 substrates. This study should be designed and conducted in accordance with the Guidance for Industry “M12 Drug Interaction Studies”.

The timetable you submitted on August 19, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 12/2026
Final Protocol Submission: 04/2027
Trial Completion: 02/2029
Final Report Submission: 06/2029

5047-5 Conduct a clinical drug interaction study to evaluate the effect of camizestrant on the pharmacokinetics of transporter substrates of P-gp and BCRP to assess the serious potential risk associated with the magnitude of exposure change, and to inform an appropriate drug interaction management strategy for coadministration of camizestrant with these transporter substrates. This study should be designed and conducted in accordance with the Guidance for Industry "M12 Drug Interaction Studies".

The timetable you submitted on August 19, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 12/2026
Final Protocol Submission: 04/2027
Trial Completion: 02/2029
Final Report Submission: 06/2029

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.[5]

Submit clinical protocol(s) to your IND 151223 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

[5] 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.

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.

PROMOTIONAL MATERIALS

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

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*.

REPORTING REQUIREMENTS

We remind you that you must comply with the 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)). The 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 Dana Kappel, Regulatory Project Manager, at (301) 796-8768 or at Dana.Kappel@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

R. Angelo de Claro, MD
Director
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

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

[6] 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/

LALEH AMIRI KORDESTANI on behalf of ROMEO A DE CLARO
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