DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Traci Dickson
Senior Manager Regulatory Affairs, Advertising and Promotion
BeOne Medicines USA, Inc.
311 Pennington-Rocky Hill Rd, Bldg 51-Ste 1358
Pennington, NJ 08534

RE: NDA 218785
BRUKINSA® (zanubrutinib) capsules, for oral use
BRUKINSA® (zanubrutinib) tablets, for oral use
MA 38

Dear Traci Dickson:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, a direct-to-consumer (DTC) broadcast advertisement (0525-BRU-PRC-138) (TV ad) for BRUKINSA® (zanubrutinib) capsules and tablets, for oral use (Brukinsa) submitted by BeOne Medicines USA, Inc. (BeOne) under cover of Form FDA 2253. FDA has determined that the TV ad is false or misleading. Thus, the TV ad misbrands Brukinsa and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The TV ad begins with an older woman looking worried with multiple images of questions and concerns presented regarding appropriateness of her treatment plan, the impact of treatment side effects on daily living, frequency of side effects, and timing of overall improvement. The voiceover states, “There’s a lot to consider when finding the best CLL [chronic lymphocytic leukemia] treatment for you. Brukinsa brings clarity to your path ahead.” The next scenes depict the woman nervously preparing to walk a long, narrow bridge. The woman is then seen cautiously walking across the bridge and using the guardrails while benefit and safety claims are both audibly and visually presented. The final scenes of the TV ad present the woman smiling and overlooking a vast landscape from a high mountaintop with her friend as the voiceover states, “See your future clearly again,” and the SUPER states, “. . . CLEARLY BRUKINSA.”

The totality of these claims and presentations misleadingly suggests that Brukinsa will allow patients to “see their futures clearly” by leaving treatment considerations or concerns aside and impacting their health-related quality of life, such as improving emotional functioning (i.e., no longer being worried or nervous) and physical functioning (i.e., having greater ability to do activities of their choosing), when this has not been demonstrated. We note that the pivotal trials, SEQUOIA and ALPINE, evaluated patients with previously untreated CLL or small lymphocytic lymphoma (SLL) and relapsed or refractory CLL/SLL, respectively, and measured patient-reported outcomes (PRO) by the European Organization for Research and Treatment of Cancer Quality of Life and the European Quality of Life Group 5-Dimension 5-

Level questionnaires. However, results from these PROs do not support the suggestion that patients on Brukinsa will "see their futures clearly" by improving their quality of life. Specifically, these data are subject to bias given the open-label trial design, were not analyzed based on a prespecified hypothesis, were not controlled for multiplicity, and thus, are considered descriptive in nature.

The TV ad also includes claims about "finding the best CLL treatment" with the patient's concerns visualized onscreen, such as "Cardiac complications concern me" and "Am I on the right treatment for me?" and it states Brukinsa is "the only BTKi [Bruton's tyrosine kinase inhibitor] proven superior to both another BTKi and to chemotherapy." This is then followed by comparisons of risk with the voiceover stating, "And Brukinsa had low rates of cardiovascular events including afib [atrial fibrillation]," and the SUPER stating, "Cardiovascular side effects ~2 years: 10% BRUKINSA vs 6% BR [bendamustine + rituximab] (grade 1-2); 21% BRUKINSA vs 30% ibrutinib (overall). Rate of atrial fibrillation (all grades): 3% BRUKINSA and BR (~2 years) 7% BRUKINSA vs 17% ibrutinib (42.5 months)." The TV ad then concludes with the presentation that patients "might do better with Brukinsa."

The totality of these claims and presentation misleadingly suggests that Brukinsa has a superior safety profile — particularly, a lower risk of cardiovascular events, including afib compared to another BTKi, specifically ibrutinib — and may be the "best" CLL treatment, when this has not been demonstrated. While the difference in the rates of atrial fibrillation (all grades) met the prespecified criteria for significance favoring Brukinsa over ibrutinib, the ALPINE trial was not sufficiently powered to demonstrate a clinically meaningful difference in the rates of atrial fibrillation or flutter between the study arms. Thus, the overall impression that Brukinsa has a lower risk of cardiovascular events, particularly atrial fibrillation relative to ibrutinib, is misleading.

The major statement includes presentations where the verbatim complete transcript or verbatim key terms or phrases from the corresponding audio do not appear in dual modality, along with presentations where there is information in the SUPERs that is not from the corresponding audio. Therefore, the TV ad is misleading because it fails to present the major statement concurrently using both audio and text (dual modality).

In addition, the major statement is presented when the TV ad's emotional story arc reaches its peak. Specifically, the woman confidently crosses the bridge and high-fives her friend. The scenes then depict the woman smiling and laughing while browsing in a gift shop with the focus shifting between various souvenirs (mugs, key chains, and hats). She then heads outdoors to overlook the mountaintop with her friend and poses for a picture. Therefore, the TV ad is misleading because these compelling and attention-grabbing visuals during the presentation of the major statement interfere with comprehension of the major statement.

Conclusion and Requested Action

For the reasons described above, the TV ad misbrands Brukinsa and makes the distribution of the drug in violation of the FD&C Act.

This letter notifies you of our concerns and provides you with an opportunity to address them. FDA requests that BeOne take immediate action to address any violations (including, for

example, ceasing and desisting promotional communications that are misleading as described above).

Please submit a written response to this letter within 15 working days from the date of receipt, addressing the concerns described in this letter, listing all promotional communications (with the 2253 submission date) for Brukinsa that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Brukinsa.

If you believe that your products are not in violation of the FD&C Act, please include in your submission to us your reasoning and any supporting information for our consideration within 15 working days from the date of receipt of this letter.

The concerns discussed in this letter do not necessarily constitute an exhaustive list of potential violations. It is your responsibility to ensure compliance with each applicable requirement of the FD&C Act and FDA implementing regulations.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. Please refer to MA 38 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. You are encouraged, but not required, to submit your response in eCTD format. All correspondence submitted in response to this letter should be placed under eCTD Heading 1.15.1.6. Additionally, the response submission should be coded as an Amendment to eCTD Sequence 5038 under NDA 218785. Questions related to the submission of your response letter should be emailed to CDER-OPDP-RPM@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Valerie Guerrier, PharmD
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

Jina Kwak, PharmD, RAC
Team Leader
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

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/

VALERIE GUERRIER
05/12/2026 10:59:38 AM

JINA KWAK
05/12/2026 11:02:09 AM