DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Nicole Van De Vaarst
Senior Manager, U.S. Commercial Regulatory Affairs
Bristol-Myers Squibb
3401 Princeton Pike
Lawrenceville, NJ 08648

RE: BLA 125554
OPDIVO® (nivolumab) injection, for intravenous use
MA 5220

BLA 125377
YERVOY® (ipilimumab) injection, for intravenous use
MA 2447

Dear Nicole Van De Vaarst:

The U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, a direct-to-consumer (DTC) broadcast advertisement (1506-US-2400730) (TV ad) for OPDIVO® (nivolumab) injection, for intravenous use (Opdivo) and YERVOY® (ipilimumab) injection, for intravenous use (Yervoy) submitted by Bristol-Myers Squibb (BMS) under cover of Form FDA 2253. FDA has determined that the TV ad is false or misleading. Thus, the TV ad misbrands Opdivo and Yervoy and makes the distribution of the drugs in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The TV ad includes the following claims (in pertinent part):

- "Lung cancer isn't me. This is me" (HERO, 0:00)
- "Your life comes first… (Voice Over, 0:07)
- "This is me…" (HERO, 1:06)

These claims are accompanied by various scenes throughout the TV ad depicting three "heroes" seemingly receiving treatment in a clinical setting but as the screen zooms out, are actually in various social settings (e.g., spending time at an amusement park with a child, at a picnic with family, and making pizza with family). The totality of these representations makes the TV ad misleading by suggesting that all patients receiving Opdivo and Yervoy for advanced non-small cell lung cancer (NSCLC) can expect to engage in these activities and remain functional with little to no diminishment of or restrictions to daily activities, when this may not be the case. We acknowledge that greater than 99% of patients enrolled in the CHECKMATE-227 trial had an Eastern Cooperative Oncology Group Performance Status score of 0 or 1 at study entry; however, we are unaware of data that supports the implication

that patients can reasonably expect to maintain this same level of activity or functioning while on treatment. In fact, according to the ADVERSE REACTIONS, Clinical Trials Experience, Metastatic Non-Small Cell Lung Cancer, *First-line Treatment of Metastatic NSCLC: In Combination with Ipilimumab* section of the FDA-approved Opdivo prescribing information (PI), patients receiving Opdivo plus Yervoy experienced several adverse reactions, including fatigue (44%), decreased appetite (31%), musculoskeletal pain (27%), diarrhea/colitis (26%), dyspnea (26%), and nausea (21%) that could limit a patient's ability to participate in the activities portrayed. In addition, 58% of patients receiving Opdivo plus Yervoy experienced serious adverse reactions.

Furthermore, the TV ad is misleading by suggesting that treatment with Opdivo plus Yervoy will positively impact a patient's health-related quality of life (HRQoL) by improving their emotional functioning (i.e., no longer tired or in distress) and social functioning (i.e., greater ability to do activities of their choosing), and may allow a patient to return to their original self (i.e., "Your life comes first" and "This is me"). This impression is furthered by the change in the TV ad's lighting for each "hero" from dark to bright and each "hero's" mood transitioning from serious to happy. FDA is not aware of data to support these suggestions. If you have data to support these suggestions, please submit them to FDA for review.

The TV ad is also misleading because the attention-grabbing visuals and frequent scene changes (i.e. the first "hero" spending time with her grandson at the amusement park, the second "hero" playing frisbee with his dog, the third "hero" spending time with family and making pizza) during the presentation of the major statement interfere with the comprehension of the major statement.

Conclusion and Requested Action

For the reasons described above, the TV ad misbrands Opdivo and Yervoy 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 BMS 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 Opdivo and Yervoy that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Opdivo and Yervoy.

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 **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 5220 and MA 2447 in addition to the BLA numbers 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 6506 and 5770 under BLA 125554 and BLA 125377, respectively. 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}

George Tidmarsh, M.D., Ph.D.
Director
Center for Drug Evaluation and Research

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/

CARTER M BEACH
09/09/2025 05:14:39 PM
On behalf of George Tidmarsh, M.D., Ph.D