DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

March 9, 2026

Iovance Biotherapeutics
Attention: Justin Custer
Senior Director Regulatory Affairs
825 Industrial Road, Suite 100
San Carlos, CA 94070

RE: AMTAGVI (lifileucel)
BLA 125773/74, 75, 76, 83

Dear Mr. Custer:

The Advertising and Promotional Labeling Branch (APLB) of the U.S. Food and Drug Administration (FDA) has reviewed various promotional materials for AMTAGVI® (lifileucel) suspension, for intravenous infusion, from Iovance Biotherapeutics (Iovance) that include exploratory analyses, such as Overall Survival (OS) data, in conjunction with representations or suggestions that AMTAGVI is effective for this type of clinical benefit. The OS data, together with such representations or suggestions, are currently presented on the AMTAGVI Healthcare Provider website[1] and in the following promotional pieces:

- Sales Aid (PRC-US-00171) - Updated Core Sales Aid
- Exhibit (PRC-US-00225) - Updated Tabletop Panel
- Slides (PRC-US-00245) - Updated Speaker Slide Deck
- Slides (PRC-US-00377) - Updated Clinical Overview Slides
- Sales Aid (PRC-US-00378) - Updated Community CSA
- Exhibit (PRC-US-00461) - ASCO Booth Panels
- Exhibit (PRC-US-00395) - CVA Touchscreen
- www-website (PRC-US-00469) - Updated HCP website
- Promotional Labeling (PRC-US-00220) - AMTAGVI fact sheet
- Slides (PRC-US-00478) - AMTAGVI intro deck
- www-ecomm (PR-US-00483) - AMTAGVI referral email
- www-ecomm (PRC-US-00484) - AMTAGVI data email

The promotional materials make false or misleading claims and representations about the benefits of AMTAGVI. Thus, the promotional materials misbrand AMTAGVI within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and make its distribution violative. 21 U.S.C. 321(n); 331(a); 352(a), (n). See 21 CFR 202.1(e)(5). These violations are

[1] AMTAGVI Healthcare Provider website https://www.amtagvi.com/hcp/treatment-outcomes/efficacy/ (last accessed March 2026).

particularly concerning from a public health perspective because the promotional materials make misleading representations about AMTAGVI being more effective or having greater clinical benefit than has been demonstrated. This may cause doctors and patients to inaccurately weigh the risks versus benefits of treatment with AMTAGVI, which can be fatal or life-threatening.

Background

According to the FDA-approved prescribing information (PI) for AMTAGVI:

> AMTAGVI is a tumor-derived autologous T cell immunotherapy indicated for the treatment of adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor.

This indication was approved under accelerated approval based on objective response rate (ORR), and continued approval may be contingent upon confirmatory trials for this endpoint and demonstration of clinical benefit. This pathway can allow for earlier approval of drugs intended to treat serious conditions and fill an unmet medical need. Accelerated approval is based on an effect on a surrogate or intermediate clinical endpoint that is thought to be reasonably likely to predict clinical benefit, rather than on a direct measurement of clinical benefit. FDA has required sponsors of drugs approved under the accelerated approval pathway, including AMTAGVI, to conduct a confirmatory trial to verify and describe the clinical benefit of the drug.[2]

AMTAGVI has a BOXED WARNING regarding treatment-related mortality, prolonged severe cytopenia, severe infection, and cardiopulmonary and renal impairment. Its WARNINGS AND PRECAUTIONS also include life-threatening internal organ hemorrhage, acute respiratory failure, acute renal failure, and hypersensitivity reactions.

False or Misleading Benefit Presentation

Prescription drug advertisements and labeling (promotional communications) misbrand a drug if they are false or misleading with respect to efficacy. The determination of whether a promotional communication is misleading includes, among other things, not only representations made or suggested in the promotional communication, but also the extent to which the promotional communication fails to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the promotional communication. See section 201(n) of the FD&C Act, 21 U.S.C. 321(n).

You include representations in AMTAGVI's promotional materials suggesting that it is effective in providing OS benefits. For example, AMTAGVI's promotional materials include the headline, "**19.7% of patients were alive at 5-year follow-up**", and a graph

[2] We note that the confirmatory trial for AMTAGVI, a Phase 3 Study to Investigate Lifileucel Regimen Plus Pembrolizumab Compared with Pembrolizumab Alone in Participants with Untreated Advanced Melanoma is currently ongoing; however, this study has not been completed (*See*: https://clinicaltrials.gov/study/NCT05727904?term=NCT05727904&rank=1)

illustrating the duration of response extended to 60 months. Your presentations include data for a time-to-event endpoint from this single-arm study, which has statistical limitations that render it uninterpretable. AMTAGVI's study was designed as a multicenter, multicohort, open-label single-arm study (i.e., with no comparator arm). Efficacy for AMTAGVI was established based on ORR and duration of response. In the absence of an appropriate comparator for AMTAGVI, it is not possible to determine if the observed effect you represented is attributable to AMTAGVI or to other factor(s), such as the natural history of the disease. Consequently, your promotional advertising and labeling that represents or suggests AMTAGVI is effective in providing OS is misleading.

We acknowledge that you have the following statement (in smaller less prominent font) presented next to the OS presentations "Overall survival in this single-arm trial is descriptive and conclusions cannot be drawn." However, this statement does not sufficiently mitigate the overall misleading message about OS for AMTAGVI.

Conclusion and Requested Action

For the reasons discussed above, your promotional materials misbrand AMTAGVI within the meaning of the FD&C Act and make its distribution violative. See 21 U.S.C. 321(n), 331(a), and 352(a), (n); 21 CFR 202.1(e)(5).

This letter notifies you of our concerns and provides you with an opportunity to address them. APLB requests that you cease any violations of the FD&C Act. Within 15 working days of receipt, please submit a written response to this letter addressing the concerns described, listing all advertising and promotional labeling materials (including the dissemination/publication date and Material ID Code) for AMTAGVI that contain the same or similar representations or suggestions, and explaining your plans for discontinuation of such.

If you believe that your product is 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 constitute an exhaustive list of potential violations. It is your responsibility to ensure compliance with all applicable requirements of the FD&C Act and its implementing regulations.

Please submit your response to your eCTD under the heading 1.15.1.6 and email a copy of your response to CBERAPLB@fda.hhs.gov. We remind you that only written communications are considered official responses. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter and refer to the BLA/STN numbers.

Questions related to the submission of your response letter should be emailed to CBERAPLB@fda.hhs.gov.

Sincerely,

Melissa Mendoza, J.D.
Office Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research