DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Petya Krasteva, Assistant General Counsel
Commercial Legal and Corporate Affairs
Daiichi Sankyo, Inc.
211 Mt. Airy Road
Basking Ridge, NJ 07920

RE: NDA 211810
TURALIO® (pexidartinib) capsules, for oral use
MA 253

Dear Petya Krasteva:

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) Turalio "Patient Ambassador Video_2025 BW Label Update" (PP-US-TU-1308) (video) for TURALIO® (pexidartinib) capsules, for oral use (Turalio) submitted by Daiichi Sankyo, Inc. (Daiichi Sankyo) under cover of Form FDA 2253. FDA has determined that the video is false or misleading. Thus, the video misbrands Turalio and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The video includes a patient testimonial, which starts with the patient "Siobhan" sitting on a deck near her garden. She reflects on how much she enjoys gardening, stating that it "brings me a lot of joy," then a blue and green animated dragonfly transitions the viewer to an animated flashback. In this animated flashback, Siobhan is seen kneeling and picking strawberries in a bright and colorful garden. She describes how she started to have difficulty standing up after kneeling in the garden, then vines are shown wrapping around her leg and arm and pulling her to the ground as the music tenses and the garden dies. The next scenes include a dark and muted garden, cold wintery weather, and suspenseful music. After her diagnosis of tenosynovial giant cell tumor (TGCT), she describes her challenges with daily activities such as getting into a car, getting up from a chair, and kneeling down to garden, while stating, "Everything was difficult." The scene starts to shift, and she's in a dark tunnel with a bright light shining through the entrance while being held in place by numerous vines. The blue and green dragonfly reappears and helps release her from the vines while Siobhan states, "… I learned about an FDA approved treatment called Turalio." In addition, the scene includes the indication in SUPER (i.e., "For adult patients with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery."). The dragonfly guides her towards the light, while she smiles and skips, and states, "It really made me feel beyond hopeful." The vines still try to attack her as she leaves the tunnel, but they are not able to hold on to her or hold her back like before. In addition, the music during this scene shifts to a light and airy sound. In the final animated scene, Siobhan

is out of the tunnel and back into the bright and colorful garden. The music is upbeat, flowers are blooming, and the vines retreat and disappear completely. The dragonfly guides her forward through the garden and she picks up her gardening basket again. The patient testimonial in the video concludes with Siobhan sitting on the deck while the blue and green dragonfly rests on a branch in front of her, and she states, "I don't know what the future holds, but I'm optimistic."

The totality of these claims and contrasting before and after presentations misleadingly suggests that treatment with Turalio will allow *all* patients to live as they did prior to their TGCT diagnosis, when this has not been demonstrated. Specifically, these claims and presentations suggest that all patients with TGCT treated with Turalio will experience a complete resolution of disease and will be able to return to daily activities (e.g., gardening), without limitations from TGCT stopping them. While the patient testimonial in this video may be an accurate reflection of this patient's own personal experience with Turalio, the testimonial does not adequately support the suggestion that other patients starting Turalio will experience a similar response.

According to the CLINICAL STUDIES section of the Turalio FDA-approved Prescribing Information (PI), in the ENLIVEN study, the Overall Response Rate (ORR) was 38% (95% CI: 27%, 50%) at Week 25 in the Turalio arm (n=61). Of the 38% of Turalio patients who responded, 15% had a complete response (CR) and 23% had a partial response. We acknowledge that "[a]t completion of the open-label extension part of the [ENLIVEN] study … the ORR using RECIST v1.1[1] was 61% (95% CI: 48%, 72%) in the 61 patients originally randomized to the TURALIO arm." However, overall, the CR is only a portion of the ORR and does not adequately support the suggestion that all patients would be able to live as they did prior to their TGCT diagnosis.

Furthermore, the totality of these claims and presentations also misleadingly suggests that treatment with Turalio will positively impact a patient's health-related quality of life by improving their emotional functioning (i.e., from feeling that "everything was difficult" to "it really made me feel beyond hopeful") and physical functioning (i.e., from vines grabbing her leg and arm to pull her down to vines not being able to grab her), and may allow a patient to return to their original self (i.e., the vines disappear and she picks up the basket to return to gardening after the dragonfly breaks her free of the TGCT vines), when this has not been demonstrated. This impression is furthered by the change in the video's mood, lighting, and music. It starts bright and colorful with light airy music. After her TGCT diagnosis, the patient has a melancholic appearance, there is suspenseful music, and the scenes are dark, cold, and muted. Then, when the dragonfly reappears and breaks her free, the patient appears happy, the music is light and airy, and the scenes are bright and colorful, similar to the beginning of the flashback. We note that the ENLIVEN study utilized PRO instruments, such

[1] Response was measured using the Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1., which defines the evaluation of target lesions as the following: Complete Response (CR): Disappearance of all target lesions. Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. See: https://ctep.cancer.gov/protocoldevelopment/docs/recist_guideline.pdf.

as Patient-Reported Outcomes Measure Information System – Physical Function (PROMIS-PF) and Worst Stiffness Numeric Rating Scale to assess patient functionality as pre-specified secondary endpoints from baseline to Week 25. However, these PRO data for PROMIS-PF and worst stiffness were uninterpretable due to the high extent of missing data (i.e., 43% for PROMIS-PF and 43% for worst stiffness) for these endpoints. Given the proportion of missing data, the results of these analyses may not reliably estimate treatment effects, and thus, valid inference cannot be made.

Therefore, these data do not support suggestions that treatment with Turalio will provide full relief from the limitations of TGCT that impact patients' daily lives or return them to a state prior to their diagnosis with TGCT. This misleading impression is especially concerning considering Turalio is associated with a Boxed Warning regarding hepatotoxicity. We acknowledge the disclaimer, "Outcomes may vary and are dependent on each patient's clinical profile and history" throughout the patient testimonial. However, inclusion of this statement in this promotional communication does not correct or mitigate the misleading suggestions regarding Turalio treatment described above.

Conclusion and Requested Action

For the reasons described above, the video misbrands Turalio 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 Daiichi Sankyo 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 Turalio that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Turalio.

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 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 253 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 3225 under NDA 211810. 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}

Rebecca Falter, PharmD, BCACP
Regulatory Review Officer
Division of Advertising & Promotion Review 1
Office of Prescription Drug Promotion

{See appended electronic signature page}

Emily Dvorsky, PharmD, RAC
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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/

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