DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Purve Patel, Head of US Regulatory Affairs
argenx US, Inc.
33 Arch Street, 32nd Floor
Boston, MA 02110

RE: BLA 761304
VYVGART HYTRULO® (efgartigimod alfa and hyaluronidase-qvfc) injection, for subcutaneous use
MA 548

Dear Purve Patel:

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) television advertisement (TV ad), (US-VYV_HYT-24-00109) for VYVGART HYTRULO® (efgartigimod alfa and hyaluronidase-qvfc) injection, for subcutaneous use (Vyvgart Hytrulo) submitted by argenx US, Inc. (argenx) under cover of Form FDA 2253. FDA has determined that the TV is false or misleading. Thus, the TV ad misbrands Vyvgart Hytrulo and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

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

- "…and while I still have CIDP, I have a chance to live vividly."
- "Vyvgart Hytrulo has been proven to significantly reduce the risk of symptoms getting worse."
- "I'm hitting fairways with the fellas. I'm hitting the road with my number one. That's how we live vividly with Vyvgart Hytrulo"

These claims are accompanied by various presentations of two CIDP patients throughout the TV ad. Specifically, one patient is shown walking to a car with a cane. She is later shown driving the car, pulling up to several food trucks, and walking to meet up with friends. Another patient, wearing braces around his lower legs, is shown walking to a golf cart to select a club, swinging the golf club, and later is shown bending down to line up and then putt a golf ball towards the hole. This scene eventually transitions to the patient walking along the golf course with friends and then eating a meal at a table overlooking the golf course.

The totality of these claims and presentations create a misleading impression that all patients with CIDP, while on treatment with Vyvgart Hytrulo, can expect to engage in these activities (e.g., playing golf, driving a car) and remain functional with little to no diminishment of or restrictions to daily activities, when this has not been demonstrated. According to the Vyvgart Hytrulo FDA-approved prescribing information (PI), CLINICAL STUDIES section, "[t]he

efficacy of VYVGART HYTRULO for the treatment of adults with chronic inflammatory demyelinating polyneuropathy (CIDP) was established in a two stage, multicenter study… The primary endpoint was the time to clinical deterioration defined as a 1-point increase in aINCAT [adjusted Inflammatory Neuropathy Cause and Treatment disability score] at two consecutive visits or a >1-point increase in aINCAT at one visit." Patients enrolled in the study had an Inflammatory Neuropathy Cause and Treatment (INCAT) disability score of ≥2, and a score of 2 had to be exclusively from leg disability. An INCAT leg disability score of 2 means that the patient usually uses unilateral support to walk outdoors. Patients in Stage B of the study had a median baseline adjusted INCAT (aINCAT) score of 3, meaning patients need unilateral support to walk outdoors or have difficulty using the hands and arms to complete tasks. While patients treated with Vyvgart Hytrulo experienced a statistically significant longer time to clinical deterioration compared to patients who received placebo, these data do not support the implications that all patients can reasonably expect to perform the level of activity depicted in the TV ad or remain functional with little to no diminishment of or restrictions to daily activities while on treatment with Vyvgart Hytrulo.

In addition, the TV ad includes the following claim:

- SUPER: "For patients identified as responders entering the main part of the study, the risk of arm and leg symptoms getting worse was 61% lower for patients taking VYVGART Hytrulo, compared to patients taking placebo (VYVGART Hytrulo=111 patients; placebo=110 patients)."

This claim is misleading because the time to clinical deterioration, the primary endpoint of the clinical trial, is not the same as the risk of worsening. According to the Vyvgart Hytrulo PI, CLINICAL STUDIES section, the hazard ratio (HR) for the time to first aINCAT increase (clinical deterioration) for patients receiving VYVGART HYTRULO compared to patients receiving placebo was 0.394. The HR is a rate measure over time of a relative risk of CIDP relapse occurring at any point during the study period. It does not show the actual risk reduction or clinical importance of the finding. The risk difference of clinical deterioration was evaluated to support the primary endpoint analysis. Based on the number of relapse events in the Vyvgart Hytrulo arm as compared to the placebo arm, patients in the Vyvgart Hytrulo arm had a reduced risk of relapse of -25.7% (95% CI, -38.0 to -11.4) compared to placebo. Therefore, the claim that "the risk of arm and leg symptoms getting worse was 61% lower for patients taking VYVGART Hytrulo…" is misleading.

Furthermore, the TV ad includes the following claims and presentations (emphasis original):

- A man golfing, who states, "And I can treat my CIDP with a once weekly injection in about 30 seconds" in conjunction with on-screen text (emphasis original), "VYVGART Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) a **once-weekly self-injection** that takes about **30 seconds"**

These claims and presentations are misleading because they suggest that the administration of Vyvgart Hytrulo can be completed in 30 seconds while participating in outdoor activities such as golfing, thereby oversimplifying the administration process. The FDA-approved Instructions for Use (IFU) for Vyvgart Hytrulo includes a number of detailed steps required for proper administration of the product, including letting the product sit on a clean, flat surface

for 30 minutes to come to room temperature, gathering necessary supplies (e.g., safety needle, alcohol swab, sharps disposal container, sterile gauze or small adhesive bandage), washing hands, injecting the medication into the abdomen, and disposing the syringe in a sharps container. We acknowledge that a small SUPER appears at the bottom of the screen stating, "See Patient Information and Instructions for Use. Monitor for allergic reactions for at least 30 minutes after injection and seek medical attention if needed." however, this does not mitigate the misleading impression.

The TV ad is also misleading because it includes claims and presentations about the uses and benefits of Vyvgart Hytrulo but omits material risk information pertaining to the warning and precautions for hypersensitivity reactions and infusion/injection-related reactions. Specifically, the major statement does not communicate the following from the "**What are the possible side effects of VYVGART HYTRULO?**" section of the Patient Information (in pertinent part; underlined emphasis added):

- "Allergic reactions: …get emergency help right away if you have any of the following symptoms of an allergic reaction: rash, swelling of the face, lips, throat or tongue, shortness of breath, trouble breathing, low blood pressure, fainting"

- "Infusion or injection-related reactions: …Tell your healthcare provider if you have any of the following symptoms of an infusion or injection-related reaction: high blood pressure, chills, shivering, chest, stomach, or back pain"

The TV ad is misleading because the attention-grabbing visuals (e.g., multiple scene changes that alternate between a man putting on a golf course, to a car stopping for a pedestrian in a crosswalk, to a woman driving a car, to four men walking on a golf course, to a woman pulling up in her car to several food trucks) and on-screen text (a car license plate "NMBR 1") 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 Vyvgart Hytrulo 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 argenx 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 Vyvgart Hytrulo that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Vyvgart Hytrulo.

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 548 in addition to the BLA 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 5543 under BLA 761304. 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}

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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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