DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Rexner Vargas
Director, Regulatory Affairs
Travere Therapeutics, Inc.
3611 Valley Centre Drive, Suite 300
San Diego, CA 92130

RE: NDA 216403
FILSPARI® (sparsentan) tablets, for oral use
MA 191

Dear Rexner Vargas:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, professional visual aid (05/2026 SPA0981 v2) for FILSPARI® (sparsentan) tablets, for oral use (Filspari) submitted by Travere Therapeutics, Inc. (Travere) under cover of Form FDA 2253. FDA has determined that the professional visual aid is false or misleading. Thus, the professional visual aid misbrands Filspari and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The professional visual aid includes the following claims (in pertinent part, bolded emphasis original, underlined emphasis added):

- **"A STRONGER FOUNDATION FOR KIDNEY PRESERVATION"** (page 1)
- "Consistent nephroprotection" (pages 1 and 3)
- "**Achieving complete remission of proteinuria (defined as <0.3 g/d) drives long-term nephroprotective benefits**" (page 2)
- "**Kidney Function Preservation**" (page 3)
- **"Nephroprotection"** (page 3)
- "**Proven to achieve better kidney function preservation over 2 years**" (page 8)
- **"FILSPARI®: a stronger foundation for kidney preservation"** (page 13)
- "Proven to achieve **better kidney function preservation**" (page 13)

These claims create a misleading impression regarding the benefits of Filspari. Specifically, claims suggesting that patients treated with Filspari will achieve kidney preservation, preservation of kidney function, or nephroprotection are misleading because these outcomes have not been demonstrated. The FDA-approved prescribing information (PI) states that Filspari "is indicated to slow kidney function decline in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk for disease progression" (underlined emphasis added). The CLINICAL STUDIES section of the PI reports that Filspari "reduced the rate of decline in

kidney function from baseline to Week 110 compared to irbesartan. The mean eGFR slope from baseline to Week 110 was -3.0 mL/min/1.73 m² per year for Filspari and -4.2 mL/min/1.73 m² per year for irbesartan…" (underlined emphasis added). While Filspari demonstrated slowing of the rate of kidney function decline relative to irbesartan, kidney function continued to decline in patients receiving Filspari. Therefore, claims suggesting that treatment with Filspari will result in kidney preservation, kidney function preservation, or nephroprotection are misleading.

The professional visual aid includes the following claims and presentation (in pertinent part, bolded emphasis original, underlined emphasis added):

- a bar graph with the heading "**Proven to drive 3x more patients to complete remission of proteinuria (<0.3 g/day)**" (page 7)

- "Proven to drive **3x more patients to complete remission of proteinuria**" (page 13)

These claims and presentation create a misleading impression regarding the efficacy of Filspari. Specifically, these claims suggest that Filspari was proven to drive three times more patients to complete remission of proteinuria when this has not been demonstrated. Filspari was demonstrated to slow kidney function decline in adults with primary IgAN who are at risk for disease progression by the change from baseline in urine protein/creatinine ratio (UPCR) and the rate of change in eGFR over a 110-week period. Complete remission of proteinuria was evaluated as an exploratory endpoint (i.e., hypothesis-generating) and as such, no alpha was allocated to this analysis, meaning no pre-specified false positive error rate was established. Accordingly, it is not possible to ascertain whether this finding is attributable to treatment with Filspari or merely due to chance. Therefore, these exploratory data do not support conclusory claims that Filspari is proven to drive complete remission of proteinuria. We acknowledge the disclaimer on page seven, "Prespecified exploratory analysis: percentage of patients with complete remission of proteinuria at any time during treatment in the double-blind period," however, this does not mitigate the misleading impression.

Page 10 of the professional visual aid includes the headline claim, "**FILSPARI was well tolerated over 2 years**" (emphasis original). This claim misleadingly minimizes the risks associated with Filspari. Specifically, according to its PI, Filspari is associated with multiple serious risks, including Boxed Warnings due to its risks of hepatotoxicity and embryo-fetal toxicity. In addition, due to the risk of hepatoxicity, Filspari has limited availability only through a restricted distribution program called the FILSPARI Risk Evaluation and Mitigation Strategy (REMS). The minimization of the serious risk of hepatotoxicity is further exacerbated by the claim on page 10, "**No drug-induced liver injury** following treatment with Filspari" in conjunction with an image of a liver (emphasis original). However, we note that there were cases of drug-induced liver injury (DILI) with hepatocellular injury patterns, indicating direct damage to liver cells. Thus, due to this serious safety concern, regular liver monitoring is required via a REMS while on treatment. We acknowledge that information regarding the risks of Filspari is presented throughout the visual aid; however, this does not mitigate the misleading minimization of the risks associated with Filspari described above.

Furthermore, page 11 of the professional visual aid includes a graph depicting mean systolic and diastolic blood pressure over 110 weeks with the headline, **"Blood pressure remained consistent over a 2-year period and was comparable to irbesartan**" (bolded emphasis original). This claim and presentation also misleadingly minimize the risks associated with Filspari by suggesting that treatment with Filspari will not adversely affect a patient's blood pressure. However, the WARNINGS AND PRECAUTIONS, Hypotension section of the Filspari PI states, "In clinical trials, there was a greater incidence of hypotension-associated adverse events, some serious, including dizziness, in patients treated with FILSPARI compared to irbesartan." Therefore, the suggestion that treatment with Filspari will not adversely affect a patient's blood pressure is misleading. We acknowledge that the information regarding the risk of hypotension is presented on pages 10 and 15; however, this does not mitigate the misleading minimization of the risk of hypotension.

Conclusion and Requested Action

For the reasons described above, the professional visual aid misbrands Filspari 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 Travere 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 Filspari that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Filspari.

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 191 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 5183 under NDA 216403. 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}

Koung Lee, RPh, MSHS
Regulatory Review Officer
Division of Advertising & Promotion Review 1
Office of Prescription Drug Promotion

{See appended electronic signature page}

Susannah O'Donnell, MPH, RAC
Deputy Director (Acting)
Division of Advertising & Promotion Review 1
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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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