your animal patients, what factors have influenced your decision (*e.g.,* legal issues surrounding cannabis, safety concerns, effectiveness concerns, product quality concerns, not found a need, etc.)? If you do not use or recommend hemp-derived cannabis products for your animal patients for reasons other than effectiveness concerns, are there any indications and species for which you believe they could be effective and why?

Dated: January 10, 2025.

P. Ritu Nalubola,

Associate Commissioner for Policy.

[FR Doc. 2025–00945 Filed 1–15–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2024–N–5933]

Proposal to Refuse to Approve a New Drug Application for TRADIPITANT; Opportunity for a Hearing

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Director of the Center for Drug Evaluation and Research (Center Director) at the Food and Drug Administration (FDA or Agency) is proposing to refuse to approve a new drug application (NDA) submitted by Vanda Pharmaceuticals, Inc. (Vanda), for TRADIPITANT capsules, 85 milligrams (mg), in its present form. This notice summarizes the grounds for the Center Director's proposal and offers Vanda an opportunity to request a hearing on the matter.

DATES: Either electronic or written requests for a hearing must be submitted by February 18, 2025; submit data, information, and analyses in support of the hearing and any other comments by March 17, 2025.

ADDRESSES: You may submit hearing requests, documents in support of the hearing, and any other comments as follows. Please note that late, untimely filed requests and documents will not be considered. The *https://www.regulations.gov* electronic filing system will accept hearing requests until 11:59 p.m. Eastern Time at the end of February 18, 2025, and will accept documents in support of the hearing and any other comments until 11:59 p.m. Eastern Time at the end of March 17, 2025. Documents received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before these dates.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov*. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov*.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2024–N–5933 for ''Proposal To Refuse To Approve a New Drug Application for TRADIPITANT; Opportunity for a Hearing.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov*. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf*.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Tereza Hess, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 202–768–5659, *tereza.hess@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Proposal To Refuse To Approve NDA 218489

Vanda submitted NDA 218489 for TRADIPITANT capsules, 85 mg, on September 18, 2023, pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(b)(1)). Vanda proposed that TRADIPITANT capsules be indicated for ''the treatment of [symptoms of] or [nausea in] in gastroparesis.''

To support a demonstration of substantial evidence of effectiveness, Vanda referred to two randomized, double-blind, placebo-controlled studies (Study 2301 and Study 3301, Group 1), and the following additional data submitted as confirmatory evidence: (1)

post hoc pooled analyses of Study 2301 and Study 3301, Group 1; (2) an open-label study (Study 3301, Group 2); (3) data from individual patient expanded access uses; and (4) two studies in a different condition (Study 2401 and Study 3401 in motion sickness). Further, Vanda proposed that Study 2301 alone and Study 3301 alone each meet the standard for substantial evidence of effectiveness. To support a demonstration of the safety of TRADIPITANT for the treatment of gastroparesis, Vanda referred to the clinical studies described above and to nonclinical studies, including in vitro studies using new alternative methods, that have been completed.

On September 18, 2024, the Office of Immunology and Inflammation (OII) in CDER issued a complete response letter to Vanda under § 314.110(a) (21 CFR 314.110(a)) stating that NDA 218489 could not be approved in its present form because the application does not provide substantial evidence of effectiveness for TRADIPITANT and does not demonstrate that the drug is safe for the proposed conditions of use. The complete response letter described the specific deficiencies that led to this determination and, where possible, recommended ways that Vanda might remedy these deficiencies. Those deficiencies are summarized below.

1. The following deficiencies in Study 3301, Group 1, and Study 2301 preclude a finding of substantial evidence of effectiveness:

a. The results of Study 3301, Group 1 (a phase 3 study) did not demonstrate a statistically significant difference between TRADIPITANT and placebo for the primary endpoint of the change from baseline to Week 12 in biweekly average nausea severity, nor did they demonstrate a nominally significant difference on nausea severity for any of the 2-week intervals assessed. In addition, there were no nominally significant differences between TRADIPITANT and placebo for the multiplicity-controlled secondary endpoints that assessed individual signs and symptoms of gastroparesis, nor for other clinically relevant endpoints such as nausea-free days. The estimated difference between TRADIPITANT and placebo for these endpoints was generally close to zero, except for the nausea-free days endpoint, which numerically favored placebo at Week 12.

b. The post hoc analyses of the results of Study 3301, Group 1 did not demonstrate a consistent benefit in reduction of nausea nor do they overcome the lack of efficacy observed on the multiple prespecified endpoints in Study 3301, Group 1. These post hoc analyses were neither controlled for multiplicity nor prespecified in the statistical analysis plan (SAP). The lack of both control for multiplicity and prespecification for the post hoc analyses greatly increases the chance of erroneously concluding a drug has an effect on an outcome when no effect exists, which is especially problematic in the context of a trial that did not demonstrate statistical significance on the primary endpoint and multiplicity-controlled secondary endpoints, such as Study 3301, Group 1.

c. Although the results of Study 2301 (a phase 2 study) demonstrated a statistically significant difference in the primary endpoint of change from baseline to Day 28 (Week 4) in the weekly average of individual daily nausea severity scores, the results were not persuasive because there were methodological shortcomings with the analysis that could bias results (*e.g.,* use of methods not in accordance with those described (or specified) in the SAP) and statistical analyses that addressed these concerns were not robust with respect to missing data assumptions. In addition, although several of the secondary endpoints were reported as having nominally statistically significant results at Day 28 (Week 4), these analyses were not controlled for multiplicity. The secondary efficacy endpoints also had the same methodological shortcomings as the primary efficacy endpoint. Furthermore, these results from Study 2301 were not supported by Study 3301, Group 1 as the latter did not achieve statistical significance on primary and secondary endpoints that were similar to those assessed in Study 2301, including at Week 4.

2. The data submitted as confirmatory evidence are not sufficient to constitute confirmatory evidence of either Study 3301, Group 1 or Study 2301. The post hoc pooled analyses of Study 3301, Group 1 and Study 2301 do not provide independent substantiation of the results of Study 2301; rather, the results of the post hoc analyses are driven by Study 2301. Additionally, the data and analysis provided from open-label sources (*i.e.,* Study 3301 Group 2, and individual patient expanded access use) are limited in their ability to support conclusions related to symptomatic improvement. Further, studies from the ongoing motion sickness program are not appropriate sources of additional efficacy data to provide confirmatory evidence for gastroparesis.

3. The application does not establish that data from either Study 3301, Group 1 or Study 2301 demonstrate substantial evidence of effectiveness on its own. As noted above, Study 3301, Group 1 did not achieve statistical significance on primary and secondary endpoints that were similar to those assessed in Study 2301, including at Week 4. Study 2301 does not provide substantial evidence of effectiveness as a single adequate and well-controlled trial due to the methodological shortcomings and limitations of the results of the trial.

4. The clinical safety data submitted with the application are inadequate to characterize the safety of TRADIPITANT for treating patients with gastroparesis. The clinical safety database included controlled clinical trial data that were limited to 12 weeks in duration. Additional longer-term safety data are needed, in part, to inform the safe use of the drug because gastroparesis is a chronic condition that necessitates ongoing daily use or recurrent intermittent treatment over months to years in most patients.

5. The nonclinical safety data submitted with the application are inadequate to characterize the safety of TRADIPITANT for treating patients with gastroparesis. The provided in vitro studies along with the provided animal studies did not adequately characterize the long-term safety of TRADIPITANT to inform risk to humans.

These deficiencies preclude a finding that the application provides substantial evidence of effectiveness for TRADIPITANT, and that the application demonstrates that TRADIPITANT is safe, for the proposed conditions of use. The complete response letter stated that to address the deficiencies, OII recommends that Vanda leverage existing data to inform the design of two new adequate and well-controlled trials in adults with idiopathic or diabetic gastroparesis. OII also recommended that Vanda conduct a chronic repeat-dose toxicity study in a nonrodent species, which would support the clinical trials longer than 12 weeks in duration.

The complete response letter stated that Vanda is required either to resubmit the application, fully addressing all deficiencies listed in the letter, or take other actions available under § 314.110 (*i.e.,* withdraw the application or request an opportunity for a hearing).

Following the complete response letter, in a letter dated November 25, 2024, Vanda indicated that it wished to receive approval of its application or a notice of opportunity for a hearing. For the reasons described above, CDER cannot approve the application in its current form; thus, we are providing Vanda with this notice of opportunity for a hearing.

II. Notice of Opportunity for a Hearing

For the reasons stated above and as explained in the September 18, 2024, complete response letter, notice is given to Vanda and all other interested persons that the Center Director proposes that FDA issue an order refusing to approve NDA 218489 under section 505(c) of the FD&C Act, on the grounds that the application fails to meet the criteria for approval under section 505(d) of the FD&C Act because there is a lack of substantial evidence that the drug is effective, and the drug has not been shown to be safe, for the proposed conditions of use, including for the proposed indication of ''the treatment of [symptoms of] or [nausea in] in gastroparesis'' (sections 505(d)(4) and 505(d)(5) of the FD&C Act).[1]

Vanda may request a hearing before the Commissioner of Food and Drugs (the Commissioner) on the Center Director's proposal to refuse to approve NDA 218489. Pursuant to § 314.200(c)(1) (21 CFR 314.200(c)(1)), if Vanda decides to seek a hearing, it must file: (1) a written notice of participation and request for a hearing on or before 30 days after the notice is published in the **Federal Register** and (2) the studies, data, information, and analyses relied upon to justify a hearing, as specified in § 314.200, on or before 60 days after the date the notice is published in the **Federal Register**.

As stated in § 314.200(g), a request for a hearing may not rest upon mere allegations or denials but must present specific facts showing that there is a genuine and substantial issue of fact that requires a hearing to resolve. We note in this regard that because CDER proposes to refuse to approve NDA 218489 based on the multiple deficiencies summarized above, any hearing request from Vanda should address all those deficiencies. Failure to request a hearing within the time provided and in the manner required by § 314.200 constitutes a waiver of the opportunity to request a hearing. If a hearing request is not properly submitted, FDA will issue a notice refusing to approve NDA 218489.

[1] Section 505(d) of the FD&C Act provides that FDA shall refuse to approve an application if, among other reasons, ''upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions'' or ''there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof[.]'' Sections 505(d)(4) and 505(d)(5) of the FD&C Act.

The Commissioner will grant a hearing if there exists a genuine and substantial issue of fact or if the Commissioner concludes that a hearing would otherwise be in the public interest. See § 314.200(g)(6). If a hearing is granted, it will be conducted according to the procedures provided in 21 CFR parts 10 through 16. See 21 CFR 314.201.

Paper submissions under this notice of opportunity for a hearing should be filed in one copy, except for those submitted as ''Confidential Submissions'' (see ''Written/Paper Submissions'' and ''Instructions'' in **ADDRESSES**). Except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, submissions may be seen in the Dockets Management Staff Office between 9 a.m. and 4 p.m., Monday through Friday, and on the internet at *https://www.regulations.gov*. This notice is issued under section 505(c)(1)(B) of the FD&C Act and §§ 314.110(b)(3) and 314.200.

Dated: January 13, 2025.

Patrizia Cavazzoni,

Director, Center for Drug Evaluation and Research.

[FR Doc. 2025–01027 Filed 1–15–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2000–D–0187]

Recommendations To Reduce the Risk of Transfusion-Transmitted Malaria; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing the availability of a draft document entitled ''Recommendations To Reduce the Risk of Transfusion-Transmitted Malaria.'' The draft guidance document provides blood establishments that collect blood and blood components with FDA's revised recommendations to reduce the risk of transfusion-transmitted malaria (TTM). The guidance recommends selectively testing blood donations from donors at risk for malaria using an FDA-licensed donor screening nucleic acid test (NAT) for *Plasmodium species (spp.),* the causative agents of malaria. The draft guidance, when finalized, is intended to supersede the document entitled ''Recommendations To Reduce the Risk of Transfusion-Transmitted Malaria,'' dated December 2022.

DATES: Submit either electronic or written comments on the draft guidance by March 17, 2025 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2000–D–0187 for ''Recommendations To Reduce the Risk of Transfusion-Transmitted Malaria.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov*