



## Fanapt® Shown to be Effective in Bipolar I Disorder in Phase III Clinical Study

December 19, 2022

- *Supplemental New Drug Application (sNDA) planned for 2023*

WASHINGTON, Dec. 19, 2022 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today reported positive results in a Phase III clinical study of Fanapt® (iloperidone tablets), a novel atypical antipsychotic, in the treatment of acute manic and mixed episodes associated with bipolar I disorder in adults. Fanapt® is currently approved by the FDA for the treatment of schizophrenia in adults.

In clinical study VP-VYV-683-3201 approximately 400 volunteers with a history of bipolar I disorder suffering from a current episode of mania were randomized to receive either Fanapt® or placebo in a 1:1 ratio at clinical sites in the United States, Bulgaria and Poland. The primary endpoint measured in Week 4 of treatment was assessed by the Young Mania Rating Scale (YMRS), a rating scale of clinical severity in the core symptoms of mania. At the end of the study (Week 4), Fanapt® treated patients showed a larger improvement than placebo treated patients, and this difference was highly statistically significant ( $p=0.000008$ ).

YMRS was assessed at the end of Weeks 1, 2, 3 and 4. Statistically significant benefit in the Fanapt® group over placebo was observed as early as the Week 2 assessment. Consistent with the total YMRS score, the individual YMRS subscale items also showed improvement in the Fanapt® group versus the placebo group over the course of the 4-week study. Other outcomes, such as Clinician Global Impression of Severity (CGI-S) and Clinician Global Impression of Change (CGI-C), also achieved statistical significance ( $p=0.0005$  and  $p=0.0002$ , respectively).

"The robust clinical trial results we report today demonstrate the potential to extend the utility of Fanapt into treating adult patients with bipolar I disorder, in addition to the already marketed indication of schizophrenia," said Mihael H. Polymeropoulos, M.D., Vanda's President, CEO and Chairman of the Board. "We look forward to submitting our supplemental New Drug Application to the FDA and expanding the Fanapt franchise."

Bipolar disorder is highly prevalent in the United States, estimated to affect 2.8%<sup>1</sup>, of the U.S. adult population, a number approximately up to ten times higher than the estimated prevalence of schizophrenia<sup>2,3</sup>.

Vanda plans to submit this pivotal study data of Fanapt® for the treatment of acute manic and mixed episodes associated with bipolar I disorder in adults in a supplemental New Drug Application (sNDA) in 2023.

### References

1. Harvard Medical School, 2007. National Comorbidity Survey (NSC). (2017, August 21). Retrieved from <https://www.hcp.med.harvard.edu/ncs/index.php>.
2. Kessler, R.C., Birnbaum, H., Demler, O., Falloon, I.R., Gagnon, E., Guyer, M., Howes, M.J., Kendler, K.S., Shi, L., Walters, E., Wu, E.Q. (2005). The prevalence and correlates of nonaffective psychosis in the National Comorbidity Survey Replication (NCS-R). *Biological Psychiatry*, 58(8), 668-76. doi: 10.1016/j.biopsych.2005.04.034
3. Wu, E.Q., Shi, L., Birnbaum, H., Hudson, T., Kessler, R. (2006). Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. *Psychological Medicine*, 36(11), 1535-40. doi: 10.1017/S0033291706008191

### About Vanda Pharmaceuticals Inc.

Vanda is a leading global biopharmaceutical company focused on the development and commercialization of innovative therapies to address high unmet medical needs and improve the lives of patients. For more on Vanda Pharmaceuticals Inc., please visit [www.vandapharma.com](http://www.vandapharma.com) and follow us on Twitter @vandapharma.

### About Fanapt®

For full U.S. Prescribing Information for Fanapt®, including indication, Boxed Warnings and Important Safety Information, visit our Web site at [www.fanapt.com](http://www.fanapt.com).

### Important Safety Information

Fanapt® needs to be taken as directed starting at a low dose and slowly increasing the strength. This may delay the control of symptoms in the first 1 to 2 weeks of treatment.

### Boxed Warning: Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Fanapt® is not approved for use in patients with dementia-related psychosis.

### Contraindications

- Known hypersensitivity to Fanapt® or to any components in the formulation. Anaphylaxis, angioedema, and other hypersensitivity reactions have been reported.

## Warnings And Precautions

- Fanapt® is not approved for treatment of patients with dementia-related psychosis. There was a higher incidence of cerebrovascular adverse events, including death, compared to placebo-treated patients.
- QT prolongation: Fanapt® prolongs QT interval and may be associated with arrhythmia and sudden death—consider using other antipsychotics first. Avoid use of Fanapt® in combination with other drugs that are known to prolong QTc; use caution and consider dose modification when prescribing Fanapt® with other drugs that inhibit Fanapt® metabolism. Monitor serum potassium and magnesium in patients at risk for electrolyte disturbances.
- Neuroleptic malignant syndrome, a potentially fatal symptom, has been reported in association with antipsychotic drugs including Fanapt®. Manage with immediate discontinuation of drug, treatment if needed, and close monitoring.
- Tardive dyskinesia: The risk of tardive dyskinesia may increase as the duration of treatment and total cumulative dose increases. Discontinue Fanapt® if clinically appropriate.
- Metabolic changes: Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and weight gain. Monitor patients for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Monitor glucose regularly in patients at risk for diabetes. Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. Weight gain has been reported; monitor weight.
- Seizures: Use Fanapt® cautiously in patients with a history of seizures or with conditions that lower seizure threshold.
- Orthostatic hypotension: Dizziness, tachycardia, and syncope can occur with standing. More rapid titration would be expected to increase the rate of orthostatic hypotension and syncope.
- Fanapt® may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls causing fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments initially and recurrently during therapy.
- Leukopenia, neutropenia, and agranulocytosis have been reported with antipsychotics. Patients with a pre-existing low white blood cell count (WBC) or a history of leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and should discontinue Fanapt® at the first sign of a decline in WBC in the absence of other causative factors.
- Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, Fanapt® elevates prolactin levels. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds.
- Body temperature regulation: Appropriate care is advised when prescribing Fanapt® for patients who will be experiencing conditions which may contribute to an elevation in core body temperature.
- Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Fanapt® should be used cautiously in patients at risk for aspiration pneumonia, including the elderly and those with advanced Alzheimer's dementia.
- Suicide: Closely supervise high-risk patients.
- Priapism: Cases have been reported in association with Fanapt® treatment.
- Potential for cognitive and motor impairment: Use caution when operating machinery.

## Adverse Reactions

- Commonly observed adverse reactions (incidence  $\geq 5\%$  and 2-fold greater than placebo) were: dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia, and weight increased.

## Drug Interactions

- The dose of Fanapt® should be reduced by one-half in patients co-administered a strong CYP2D6 or CYP3A4 inhibitor.

## Use In Specific Populations

- Fanapt® may cause extrapyramidal symptoms and/or withdrawal symptoms in neonates with third trimester exposure. Nursing mothers are advised not to breastfeed while taking Fanapt®.
- The safety and effectiveness of Fanapt® has not been established in children and adolescents.
- Fanapt® is not recommended for patients with severe hepatic impairment.
- The dose of Fanapt® should be reduced by one-half in patients who are poor metabolizers of CYP2D6.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements in this press release, including, but not limited to statements regarding Vanda's clinical development plan and strategies for Fanapt® for the treatment of acute manic and mixed episodes associated with bipolar I disorder in adults, the efficacy of Fanapt®, the potential therapeutic opportunity for Fanapt® and the prevalence of bipolar disorder are "forward-looking statements" under the securities laws. Forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Important factors that could cause actual results to differ materially from those reflected in Vanda's forward-looking statements include, among others, the ability of Fanapt® to safely and effectively treat acute manic and mixed episodes associated with bipolar I disorder in adults, Vanda's ability to submit the sNDA for Fanapt® in 2023, Vanda's ability to obtain regulatory approval for Fanapt® in the treatment of acute manic and mixed episodes associated with bipolar I disorder in adults and the actual number of adults in the U.S. affected by bipolar disorder. There can be no assurance that the actual results or developments anticipated by Vanda will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, Vanda. Therefore, no assurance can be given that the outcomes stated in such forward-looking statements and estimates will be achieved. Forward-looking statements in this press release should be evaluated together with the various risks and uncertainties that affect Vanda's business and market, particularly those identified in the "Cautionary Note Regarding Forward-Looking Statements", "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Vanda's Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as updated by Vanda's subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the U.S. Securities and Exchange Commission, which are available at [www.sec.gov](http://www.sec.gov).

All written and verbal forward-looking statements attributable to Vanda or any person acting on its behalf are expressly qualified in their entirety by the cautionary statements contained or referred to herein. Vanda cautions investors not to rely too heavily on the forward-looking statements Vanda makes or that are made on its behalf. The information in this press release is provided only as of the date of this press release, and Vanda undertakes no obligation, and specifically declines any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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