Vanda Pharmaceuticals Announces FDA Approval of BYSANTI™ (milsaperidone) for the treatment of Bipolar I Disorder and Schizophrenia - A New Chemical Entity Opening New Horizons in Psychiatric Innovation

February 20, 2026

WASHINGTON, Feb. 20, 2026 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Nasdaq: VNDA) today announced that the U.S. Food and Drug Administration (FDA) has approved BYSANTI™ (milsaperidone) tablets, a first line therapy for the acute treatment of manic or mixed episodes associated with bipolar I disorder and for the treatment of schizophrenia in adults.

BYSANTI™ is a new chemical entity (NCE) that belongs in the class of atypical antipsychotics. In clinical studies BYSANTI™ demonstrated bioequivalence to iloperidone across the therapeutic dosing spectrum enabling it to leverage well-established knowledge of efficacy and safety derived from a rich clinical development program and more than 100,000 patient-years of real-world experience with Fanapt® (iloperidone). As such BYSANTI™ represents a novel therapeutic option with a trusted safety profile in the treatment of these serious psychiatric conditions.

"The BYSANTI™ approval marks a significant step forward, offering patients and providers a reliable new treatment grounded in extensive clinical heritage," said Mihael H. Polymeropoulos, M.D., President, CEO and Chairman of the Board of Vanda Pharmaceuticals. "BYSANTI™ exemplifies a new era of accelerated innovation in drug development that can transform how we address unmet needs in behavioral health."

BYSANTI™ is currently being tested as a once-daily adjunctive treatment in treatment-resistant major depressive disorder in an ongoing clinical study expected to complete by the end of this year.

BYSANTI™ (milsaperidone), a new chemical entity, rapidly interconverts to iloperidone, providing dual active molecules that work in tandem by antagonizing dopamine D2, serotonin 5-HT2A, and alpha1-adrenergic receptors to modulate key pathways in these disorders. Its safety profile aligns closely with that established for iloperidone.

BYSANTI™'s unique in-class receptor binding profile, featuring strong alpha-adrenergic binding in excess of dopamine and serotonin receptor binding, makes it suitable for further investigation in conditions that include symptoms of hostility, agitation, and hyperarousal.

Vanda anticipates commercial availability of BYSANTI™ in Q3 of 2026. BYSANTI™ marketing exclusivity is expected to be protected by regulatory data exclusivity and issued US patents, with the latest expiring in 2044, providing a robust foundation for long-term innovation and patient benefit.

BYSANTI™ is the second new drug approval for Vanda in less than 2 months following the approval of NEREUS™ in December of 2025.

About BYSANTI™

To access the full Prescribing Information, including BOXED WARNING, visit www.bysanti.com.

About Bipolar I Disorder and Schizophrenia

Bipolar I disorder impacts a significant portion of the roughly 10 million Americans with bipolar disorder, characterized by manic or mixed episodes that require effective symptom management to enhance outcomes.[1] Schizophrenia affects approximately 1% of the U.S. adult population (about 2.8 million people), often causing substantial functional impairment, frequent hospitalizations, and diminished quality of life.[2345]

References

1. Harvard Medical School, 2007. National Comorbidity Survey (NSC). (2017, August 21).
2. Potkin SG, et al. Efficacy of iloperidone in the treatment of schizophrenia: initial phase 3 studies. *J Clin Psychopharmacol.* 2008;28(2 Suppl 1):S4-S11. doi:10.1097/JCP.0b013e3181692787.
3. Cutler AJ, et al. Four-week, double-blind, placebo- and ziprasidone-controlled trial of iloperidone in patients with acute exacerbations of schizophrenia. J Clin Psychopharmacol. 2008;28(2 Suppl 1):S20-S28. doi:10.1097/JCP.0b013e318169278d.
4. Weiden PJ, et al. A Randomized Trial of Iloperidone for Prevention of Relapse in Schizophrenia: The REPRIEVE Study. J Clin Psychopharmacol. 2016;36(4):302-308. doi:10.1097/JCP.0000000000000516. (PMC4982888).
5. Torres R, et al. Efficacy and Safety of Iloperidone in Bipolar Mania: A Double-Blind, Placebo-Controlled Study. J Clin Psychiatry. 2024;85(1):23m14966. doi:10.4088/JCP.23m14966.

INDICATION AND IMPORTANT SAFETY INFORMATION

BYSANTI™ (milsaperidone) is an atypical antipsychotic indicated for the treatment of schizophrenia in adults and the acute treatment of manic or mixed episodes associated with bipolar I disorder in adults.

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. BYSANTI™ is not approved for use in patients with dementia-related psychosis.

CONTRAINDICATIONS

- Known hypersensitivity to milsaperidone or the inactive ingredients in BYSANTI™.

WARNINGS AND PRECAUTIONS

- Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack).
- QTc Interval Prolongation: may be associated with torsade de pointes and sudden death. Avoid concomitant use of BYSANTI™ with other drugs that prolong the QTc interval, and in patients with a significant risk of developing torsade de pointes; consider decreasing the BYSANTI™ dosage when prescribing BYSANTI™ with other drugs that inhibit milsaperidone metabolism or in CYP2D6 poor metabolizers. Monitor serum potassium and magnesium at baseline and during treatment in patients at risk for significant electrolyte disturbances.
- Neuroleptic Malignant Syndrome (NMS): If NMS is suspected, immediately discontinue BYSANTI™ and provide intensive symptomatic treatment and close monitoring.
- Tardive Dyskinesia: Discontinue if clinically appropriate.
- Metabolic Changes: Monitor for hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain.
- Orthostatic Hypotension and Syncope: Monitor heart rate and blood pressure in patients who are vulnerable to hypotension, and in those with known cardiovascular or cerebrovascular disease.
- Seizures: Use cautiously in patients with a history of seizures or with conditions that lower seizure threshold.
- Leukopenia, Neutropenia, and Agranulocytosis: Patients with a pre-existing low white blood cell count (WBC) or absolute neutrophil count or a history of drug induced leukopenia or neutropenia should have frequent monitoring of their complete blood count during the first few months of BYSANTI™ therapy and should discontinue BYSANTI™ at the first sign of a decline in WBC in the absence of other causative factors. Discontinue BYSANTI™ in patients with absolute ANC <1000/mm3 and follow their WBC until recovery.
- Priapism: Severe priapism may require surgical intervention.
- Potential for Cognitive and Motor Impairment: Use caution about driving a motor vehicle or operating hazardous machinery until patients are reasonably certain that therapy with BYSANTI™ does not adversely affect them.
- Intraoperative Floppy Iris Syndrome (IFIS): It is not recommended to initiate therapy in patients scheduled to have cataract or glaucoma surgery. IFIS during cataract surgery may require modifications to the surgical cataract technique.
- Falls: BYSANTI™ may increase the risk of falls, which could cause fractures or other injuries.
- Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, BYSANTI™ elevates prolactin levels. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds.
- Body Temperature Regulation: Atypical antipsychotics may disrupt the body's ability to reduce core body temperature.
- Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use.

ADVERSE REACTIONS

- Commonly observed adverse reactions (incidence ≥5% and 2-fold greater than placebo) were:
    - Schizophrenia: dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia, and weight increased.
    - Bipolar mania: tachycardia, dizziness, dry mouth, hepatic enzymes increased, nasal congestion, weight increased, hypotension, and somnolence.

DRUG INTERACTIONS

- Strong CYP2D6 Inhibitors: Reduce the dosage of BYSANTI™ when administered with a strong CYP2D6 inhibitor.
- Strong CYP3A4 Inhibitors: Reduce the dosage of BYSANTI™ when administered with a strong CYP3A4 inhibitor.
- Strong CYP2D6 and Strong CYP3A4 Inhibitors: Reduce the dosage of BYSANTI™ if administered concomitantly with both a CYP2D6 and a CYP3A4 inhibitor by one-half.
- Drugs that Lower Blood Pressure: Avoid concomitant administration of BYSANTI™ with alpha-adrenergic blocking agents and consider lowering the dosage of other drugs that lower blood pressure.

USE IN SPECIFIC POPULATIONS

- CYP2D6 poor metabolizers: Consider CYP2D6 genetic testing to determine the patient's CYP2D6 metabolizer status prior to BYSANTI dosing. Follow the titration schedule for CYP2D6 poor metabolizers.
- Pregnancy: Neonates exposed to antipsychotic drugs during the third trimester of pregnancy are at risk of extrapyramidal and/or withdrawal symptoms following delivery.
- Lactation: Advise not to breastfeed during BYSANTI™ treatment and for 6 days after the last dose in CYP2D6 normal metabolizers and 8 days after the last dose in CYP2D6 poor metabolizers.
- Hepatic Impairment: BYSANTI™ is not recommended for patients with severe hepatic impairment.

To report suspected adverse reactions, contact Vanda Pharmaceuticals Inc. at 1-844-GO-VANDA (1-844-468-2632) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See full Prescribing Information including boxed warning.

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 and follow us on X @vandapharma.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements in this press release, including but not limited to statements regarding patient and provider access to BYSANTI™, develop additional indications for BYSANTI™, including treatment-resistant major depressive disorder and conditions involving hostility, agitation and hyperarousal; the prevalence of bipolar I disorder and schizophrenia; Vanda's commercial launch plans for BYSANTI™ and the timing thereof; and the potential to extend patent exclusivity for BYSANTI™ until 2044, are "forward-looking statements" under the securities laws. All statements other than

statements of historical fact are statements that could be deemed forward-looking statements. Forward-looking statements are based upon current expectations and assumptions that involve risks, changes in circumstances and uncertainties. Important factors that could cause actual results to differ materially from those reflected in Vanda's forward-looking statements include, among others, Vanda's ability to successfully execute the commercial launch of BYSANTI™ and to execute such launch within the expected timeframe; the accuracy of the estimates of the prevalence of bipolar I disorder and schizophrenia; and Vanda's ability to satisfy the conditions necessary to extend BYSANTI™'s patent exclusivity until 2044. Therefore, no assurance can be given that the 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. 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 most recent Annual Report on Form 10-K, 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.

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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