Vanda Pharmaceuticals Announces FDA Granted Orphan Drug Designation for VGT-1849B, a Novel and Selective Candidate for the Treatment of Polycythemia Vera

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WASHINGTON, Aug. 28, 2025 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today announced the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation for VGT-1849B, a selective peptide nucleic acid-based JAK2 inhibitor for the treatment of polycythemia vera (PV).

PV is a chronic myeloproliferative disorder characterized by aberrant hematopoiesis of myeloid lineage with exuberant red cell production and increased release of pro-inflammatory cytokines. More than 95% of PV patients harbor the *JAK2* V617F gain-of-function mutation leading to aberrant JAK2 production.[1] The prevalence of PV in the United States is estimated to affect 44 to 57 per 100,000 people.[2]

VGT-1849B is an antisense oligonucleotide (ASO) that utilizes a novel backbone chemistry, OliPass Peptide Nucleic Acid (OPNA), that has been derived from peptide nucleic acid (PNA) by rationally introducing cationic lipid moieties onto nucleobases. By covalently attaching cationic lipid groups onto PNA, cell permeability and affinity for RNA are markedly improved.

By selectively targeting *JAK2* mRNA, VGT-1849B reduces downstream signaling and $JAK2^{V617F}$-driven autonomous cell proliferation. VGT-1849B targets *JAK2* with high precision and effectively reduces JAK2 protein production, without any off-target kinase effects. Inhibiting JAK2 acts to suppress hematopoiesis, consequently reducing red blood cell, neutrophil, platelet, and lymphocyte production. The ability of VGT-1849B to reduce JAK2 protein may alleviate the disease burden that patients with PV face with a favorable safety profile, resulting in a higher quality of life for patients.

JAK2 inhibitors have been shown to be efficacious in treating various JAK-dependent hematologic malignancies, including the treatment of PV. While there are several JAK inhibitors available such as Jakafi®, Inrebic®, Ojjaara®, and Vonjo®, none are solely selective to JAK2. Due to the highly conserved structure of the catalytic sites of protein kinases, JAK2 inhibitors may bind to off-target kinases, leading to increased toxicity and a worse overall safety profile. The adverse side effects that may occur from JAK inhibition emphasize the importance of selectively targeting JAK2 while avoiding inhibition of other JAK family members. By specifically targeting JAK2, we aim to reduce the risk of infection and toxic effects that are seen with inhibitors that also block JAK1, JAK3, TYK2, or other kinases outside of the JAK family.

If approved, VGT-1849B could offer targeted efficacy with an improved safety profile and convenient infrequent dosing.

Orphan Drug Designation is granted by the FDA to investigational therapies addressing rare medical conditions and provides benefits to drug developers.

References

1. P. Gou, W. Zhang, and S. Giraudier, "Insights into the Potential Mechanisms of JAK2V617F Somatic Mutation Contributing Distinct Phenotypes in Myeloproliferative Neoplasms," *Myeloproliferative Neoplasms. Int. J. Mol. Sci*, vol. 2022, p. 1013, 2022, doi: 10.3390/ijms.
2. Grunwald, M. R.; Stein, B. L.; Boccia, R. V.; Oh, S. T.; Paranagama, D.; Parasuraman, S.; Colucci, P.; Mesa, R. Clinical and Disease Characteristics From REVEAL at Time of Enrollment (Baseline): Prospective Observational Study of Patients With Polycythemia Vera in the United States. Clin Lymphoma Myeloma Leuk 2018, 18 (12), 788-795.e2. https://doi.org/10.1016/j.clml.2018.08.009.

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.

About VGT-1849B

VGT-1849B is an antisense oligonucleotide (ASO) that utilizes a novel backbone chemistry, OliPass Peptide Nucleic Acid (OPNA) peptide nucleic acid, and selectively targets *JAK2* mRNA, reducing aberrant levels of JAK2 that may cause hematologic malignancies. OPNA was derived from PNA through rational chemical modifications to enhance cell permeability and RNA affinity. For therapeutic intervention, OPNA potently binds to target pre-mRNA, induces exon skipping, and yields an mRNA splice variant. Unlike other types of RNA therapeutics, OPNA does not require formulation aid for *in vivo* therapeutic activity. OPNA oligonucleotide-based therapeutics have broad applicability in addressing a number of disorders caused by genetic variants.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements in this press release, including, but not limited to statements regarding the estimated prevalence of PV in the United States, the potential therapeutic effects of VGT-1849B, the safety profile of VGT-1849B and the potential benefits of VGT-1849B 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, the accuracy of the reporting and diagnosis of PV cases, the ability of VGT-1849B to safely and effectively treat PV, the ability of VGT-1849B to provide patients with the anticipated benefits and Vanda's ability to successfully complete the clinical development of, and obtain regulatory approval for, VGT-1849B in the treatment of PV. 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.

Corporate Contact:

Kevin Moran
Senior Vice President, Chief Financial Officer and Treasurer
Vanda Pharmaceuticals Inc.
202-734-3400
pr@vandapharma.com

Jim Golden / Jack Kelleher / Dan Moore
Collected Strategies
VANDA-CS@collectedstrategies.com

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