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

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WASHINGTON, Dec. 20, 2024 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today announced the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation for VGT-1849A, a selective antisense oligonucleotide (ASO)-based JAK2 inhibitor for the treatment of polycythemia vera (PV), a form of a rare hematologic malignancy that is estimated to affect 1 in 2000 Americans.[1]

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.[2]

Inhibiting JAK2 acts to suppress hematopoiesis, consequently reducing red blood cell, neutrophil, platelet, and lymphocyte production. JAK2 inhibitors have been shown to be efficacious in treating various JAK-dependent hematologic malignancies, including the treatment of PV. By selective reduction of JAK2 levels, the ASO VGT-1849A has the potential to reduce JAK2V617F-driven pathogenic signaling, ultimately suppressing the malignant proliferation and survival of hematopoietic cells.

Currently available small molecule inhibitors targeting the JAK2 protein kinase, such as Jakafi®, Inrebic®, Ojjaara®, and Vonjo®, lack sole selectivity for the target protein, which can result in off target effects. 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, Vanda seeks to reduce the risk of infection and toxic effects that are seen with inhibitors also blocking JAK1, JAK3, TYK2, or other kinases outside of the JAK family.

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

"This orphan designation for VGT-1849A is an important milestone in precision medicine-based therapeutics in the space of hematological malignancies. This milestone marks the second precision medicine therapeutic for Vanda following the development of VCA-894A for Charcot-Marie-Tooth[3] that is expected to begin clinical testing in the coming months," said Mihael H. Polymeropoulos, M.D., Vanda's President, CEO and Chairman of the Board.

VGT-1849A is a novel ASO treatment candidate for PV and other JAK2-driven hematologic malignancies. By selectively targeting JAK2, VGT-1849A reduces downstream signaling and $JAK2^{V617F}$-driven autonomous cell proliferation, without any off-target kinase effects. The ability of VGT-1849A to reduce JAK2 activity may alleviate the disease burden that patients with PV face with a favorable safety profile, resulting in a higher quality of life for patients.

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

References:

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2. 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, https://doi.org/10.3390/ijms23031013
3. S. Smieszek, C. Tyner, A. Kaden, C. Johnson, C. Polymeropoulos, G. Birznieks, M. Polymeropoulos. Potential treatment for CMT2S caused by IGHMBP2 cryptic splice variant, with ASO based therapeutic [abstract]. Mov Disord. 2023; 38 (suppl 1). https://www.mdsabstracts.org/abstract/potential-treatment-for-cmt2s-caused-by-ighmbp2-cryptic-splice-variant-with-aso-based-therapeutic/.

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-1849A

VGT-1849A is an antisense oligonucleotide (ASO) that selectively targets JAK2, reducing increased activity of JAK2 that may cause hematologic malignancies. ASOs 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, the potential therapeutic effects of VGT-1849A, the timing of the initiation of clinical testing of VCA-894A and the potential benefits of VGT-1849A, 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 accuracy of the reporting and diagnosis of PV cases, the ability of VGT-1849A to safely and effectively treat PV, Vanda's ability to begin clinical testing of VCA-894A during the specified timeframe and Vanda's ability to successfully complete the clinical

development of, and obtain regulatory approval for, VGT-1849A in the treatment of PV. 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, 2023, 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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