



Vanda Pharmaceuticals Announces Orphan Drug Designation Granted for VCA-894A, a Novel Antisense Oligonucleotide Candidate for the Treatment of Charcot-Marie-Tooth Disease, Type 2S

June 2, 2023

WASHINGTON, June 1, 2023 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today announced the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation for VCA-894A for the treatment of Charcot-Marie-Tooth disease, axonal, type 2S (CMT2S), caused by cryptic splice site variants within IGHMBP2.

CMT2S is a rare subtype of Charcot-Marie-Tooth disease (CMT), an inherited peripheral neuropathy for which there is no available treatment. The estimated prevalence of CMT is 1 in 2,500 individuals, with varying clinical features dependent on the various genetic variants of CMT.^{1,2} The prevalence of CMT2S is estimated to be less than 1 in 1,000,000 worldwide.³

Onset of CMT2S begins in early childhood.² CMT2S is characterized by slowly progressive distal muscle weakness and atrophy, affecting the upper and lower limbs in a child's first decade of life, leaving patients with decreased reflexes and sensory impairment.^{1,2} Because CMT2S is a progressive disease, most patients become wheelchair bound.

"This designation is an important milestone, which we believe may enable the development of individualized treatments tailored to one's genetic variants for patients with CMT2S," said Mihael H. Polymeropoulos, M.D., Vanda's President, CEO and Chairman of the Board.

VCA-894A is a novel antisense oligonucleotide (ASO) with a mechanism of action that specifically targets a cryptic splice site variant within immunoglobulin mu-binding protein 2 (IGHMBP2). Mutations within IGHMBP2 play a pivotal role in the manifestation of CMT2S, likely due to alpha-motor neuron loss, and consequently peripheral nervous system deterioration.⁴ ASOs have the capacity to modulate gene expression, allowing for the personalized treatment of rare diseases. Delivery of ASOs to the central nervous system has been previously successful in several ASO programs, with a broad applicability in addressing a number of neurodegenerative and neuromuscular disorders.⁵

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

References

1. Cottenie, E., et al. (2014). Truncating and missense mutations in IGHMBP2 cause Charcot-Marie Tooth disease type 2. *American journal of human genetics*, 95(5), 590–601. <https://doi.org/10.1016/j.ajhg.2014.10.002>
2. Nam, S. H., & Choi, B-O. (2019). Clinical and genetic aspects of Charcot-Marie-Tooth disease subtypes." *Precision and Future Medicine*, 3(2), 43–68. <https://doi.org/10.23838/pfm.2018.00163>
3. (2023). *Charcot-Marie-Tooth disease type 2S*. *Orpha.net*. https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Ing=EN&Expert=443073
4. Rzepnikowska, W., & Kochański, A. (2021). Models for IGHMBP2-associated diseases: an overview and a roadmap for the future. *Neuromuscular disorders: NMD*, 31(12), 1266–1278. <https://doi.org/10.1016/j.nmd.2021.08.001>
5. Crooke, S. T., Liang, X. H., Baker, B. F., & Crooke, R. M. (2021). Antisense technology: A review. *The Journal of biological chemistry*, 296, 100416. <https://doi.org/10.1016/j.jbc.2021.100416>

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 Twitter @vandapharma.

About VCA-894A

VCA-894A is a 2'-O-methoxyethyl (MOE) phosphorothioate oligonucleotide sodium salt. VCA-894A specifically targets a cryptic splice site variant within IGHMBP2, which causes CMT2S. ASOs may have broad applicability in addressing a number of disorders, from nervous system treatments to systemic treatments.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements in this press release, including, but not limited to statements regarding the estimated prevalence of CMT and CMT2S and the development of individualized treatments, 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 CMT and CMT2S cases and the ability to successfully complete the clinical development of, and obtain regulatory approval for, VCA-894A in the treatment of CMT2S. 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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