Vanda´s Tradipitant Improves Itch and Disease Severity in Patients with Atopic Dermatitis

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-- Worst Itch Visual Analog Scale (Worst Itch VAS): Tradipitant vs. Placebo p=0.019
-- Scoring Atopic Dermatitis (SCORAD): Tradipitant vs. Placebo p=0.008
Management to host conference call on Thursday, September 14 at 8:30 AM ET

WASHINGTON, Sept. 13, 2017 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (NASDAQ: VNDA) today announced results from an 8-week randomized Phase II clinical study of tradipitant as a monotherapy in the treatment of chronic pruritus in patients with atopic dermatitis. Tradipitant was shown to improve the intensity of the worst itch patients experienced, as well as atopic dermatitis disease severity.

Atopic dermatitis is a very common skin disorder affecting millions of people worldwide. Treatment in atopic dermatitis often begins with non-pharmacologic measures and progresses to the use of topical corticosteroids, topical calcineurin inhibitors and topical PDE4 inhibitors. Systemic treatments approved by the U.S. Food and Drug Administration (the FDA) include corticosteroids and recently dupilumab, an IL-4 receptor alpha inhibitor, for moderate and severe disease. The American Academy of Dermatology (AAD) recommends that systemic corticosteroid treatment should be generally avoided because of the potential of short-term and long-term adverse reactions to these agents.

At this time, there are very few safe systemic treatments for atopic dermatitis. Vanda designed this Phase II study to assess whether the systemic administration of the oral neurokinin-1 receptor (NK-1R) antagonist, tradipitant could improve chronic pruritus and the severity of atopic dermatitis.

Tradipitant demonstrated significant and clinically meaningful improvement in a number of measures of itch. Specifically, significant improvements were observed in the measurement of Worst Itch Visual Analog Scale (VAS) (p=0.019). Tradipitant also showed significant effects in a responder analysis for Worst Itch in patients who achieved improvements of greater than or equal to 40 points improvement from baseline in Worst Itch VAS scores (p=0.037) or greater than or equal to 30 points (p=0.049). On the pre-specified primary endpoint of Average Itch VAS, tradipitant showed improvement over placebo, but this improvement was not significant due to high placebo effect and the lack of sensitivity of this measure.

Consistent with the observed improvements in Worst Itch, which is associated with scratching behavior, tradipitant also demonstrated disease modifying properties by showing significant improvement in the Total SCORAD scale (p=0.008) and Objective SCORAD scale (p=0.005). Specifically, tradipitant showed significant improvements in several clinical features of severity of atopic dermatitis, including excoriation, erythema, oozing and dryness.

These clinically meaningful effects were also accompanied by significant improvements in the Clinical Global Impression scale - Change (CGI-C) (p=0.007), the Patient Global Impression scale (PGI-C) Itch (p=0.024) the PGI-C AD (p=0.007). Similarly, tradipitant also showed direct patient reported benefits as measured by the Patient Benefit Index scale (PBI) (p=0.037).

"We are extremely pleased with the outcome of this study where clinically meaningful differences were observed not just in the symptom of the worst itch in patients suffering from atopic dermatitis but also in measures of disease severity. We believe that tradipitant's ability to significantly help the underlying pathophysiology of atopic dermatitis represents a potentially significant medical advance in treating these patients," said Mihael H. Polymeropoulos, MD, Vanda's President and CEO.

"It's exciting to see results here with significant and highly meaningful improvements in both worst itch as well as a recovery in the lesions for patients in the study," said Gil Yosipovitch, MD, Professor of Dermatology, Miller School of Medicine, and Director of the Miami Itch Center at the University of Miami as well as an investigator in this study. "These results over 8 weeks provide further confirmation that breaking the itch-scratch cycle causing neural sensitization can have a profound benefit for patients and help ameliorate atopic dermatitis itself. Today, there are limited treatment options for the many patients who suffer from atopic dermatitis, making this study outcome a very promising step towards becoming a major advancement in the armamentarium for physicians."

In this Phase II study, 168 patients were randomized 1:1 to receive either tradipitant 85 mg BID or placebo for a period of 8 weeks. Entry criteria included patients suffering from moderate or severe itching with mild to severe atopic dermatitis excluding only the most severe patients with an upper limit of 80 on total SCORAD (average baseline total SCORAD=47).Tradipitant was found to be safe and well tolerated with minimal adverse events recorded.

Vanda believes that if these results are further confirmed in future studies, tradipitant has the potential to become a first line pharmacological option in the treatment of patients with atopic dermatitis in need of systemic treatment. The detailed results of this study are expected to be presented in upcoming meetings and prepared for peer reviewed publications.

In addition, Vanda expects to meet with the FDA in the near future to further define and confirm the clinical development path towards registration of tradipitant in the treatment of patients with atopic dermatitis.

Study 2102 Results Summary

Continuous	*ITT population*				
		Tradipitant	Placebo	Diff	p-value
A. Itch Outcomes	Average Itch VAS	-41.5	-35.8	-5.7	0.306
	Worst Itch VAS	-44.2	-30.6	-13.6	0.019
	Worst Itch NRS Night	-3.4	-2.4	-1.1	0.029
	Worst Itch NRS Day	-3.3	-2.5	-0.8	0.074
B. Disease Outcomes	SCORAD Total	-21.3	-13.6	-7.7	0.008

	Objective SCORAD	-13.3	-7.2	-6.1	0.005
	Subjective SCORAD	-8.1	-6.7	-1.4	0.157
C. General Impression Outcomes	CGI-C	2.6	3.3	-0.7	0.007
	PGI-C Itch	2.6	3.2	-0.6	0.025
	PGI-C AD	2.7	3.4	-0.7	0.007
D. Quality of Life Outcomes	PBI	1.7	1.2	0.5	0.038
	SKINDEX 16	-34.8	-26.6	-8.2	0.102
Categorical	*ITT population*				
		Tradipitant	Placebo	Diff	p-value
A. Itch Outcomes	Worst Itch VAS >=40	52.6%	34.7%	17.9%	0.037
	worst Itch VAS >=30	56.6%	38.9%	17.7%	0.049
B. Disease Outcomes	SCORAD >=50%	44.0%	20.8%	23.2%	0.004
	EASI >=75%	21.1%	11.1%	10.0%	0.067

Further data and tables can be found at http://mma.prnewswire.com/media/555779/VLY_Plots_Final.pdf

Conference Call

The Vanda management team will host a conference call and live webcast tomorrow, September 14, 2017, at 8:30 AM ET to discuss these updates. Investors can call 1-888-771-4371 (domestic) or 1-847-585-4405 (international) and use passcode 45656982. A replay of the call will be available on Thursday, September 14, 2017, beginning at 11:00 AM ET and will be accessible until Thursday, September 21, 2017, at 11:59 PM ET. The replay call-in number is 1-888-843-7419 for domestic callers and 1-630-652-3042 for international callers. The passcode number is 45656982.

The conference call will be broadcast simultaneously on Vanda's website. Investors should click on the Investor Relations tab and are advised to go to the website at least 15 minutes early to register, download, and install any necessary software or presentations. The call will also be archived on Vanda's website for a period of 30 days.

About Atopic Dermatitis and Chronic Pruritus

Atopic dermatitis is a common chronic, relapsing inflammatory skin disorder characterized by the symptom of intense and persistent pruritus or itch. Other clinical features include erythema, excoriation, edema, lichenification, oozing and xerosis.

About the Neurokinin-1 Receptor and Substance P

The NK-1R is expressed throughout different tissues of the body, with major activity found in neuronal tissue. SP and NK-1R interactions in neuronal tissue regulate neurogenic inflammation locally and the pain perception pathway through the central nervous system. Other tissues, including endothelial cells and immune cells, have also exhibited SP and NK-1R activity (2). The activation of NK-1R by the natural ligand SP is involved in numerous physiological processes, including the perception of pain, behavioral stressors, cravings and the processes of nausea and vomiting (1,2,3). An inappropriate over-expression of SP, either in nervous tissue or peripherally, could result in pathological conditions such as substance dependence, anxiety, nausea/vomiting and pruritus (1,2,3,4). An NK-1R antagonist may possess the ability to reduce this over-stimulation of the NK-1R, and as a result address the underlying pathophysiology of the symptoms in these conditions.

About Tradipitant

Tradipitant is an NK-1R antagonist licensed by Vanda from Eli Lilly and Company (Lilly) in April 2012. Tradipitant is currently in clinical development for chronic pruritus in patients with atopic dermatitis. Previous research at Lilly focused on the potential of tradipitant as a novel therapeutic in alcohol dependence (1). The patent describing tradipitant as a new chemical entity is expected to expire in the United States in June 2029 based on an anticipated Hatch-Waxman patent term extension and expires worldwide in April 2023 absent any other applicable patent term adjustments.

About Vanda

Vanda is a 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.

Abbreviations

BID	Twice daily
CGI-C	Clinical Global Impression of Change
EASI	Eczema Area and Severity Index
NK-1R	Neurokinin-1 Receptor
NRS	Numerical Rating Scale
PBI	Patient Benefit Index
PGI-C AD	Patient Global Impression of Change Atopic Dermatitis specific
PGI-C Itch	Patient Global Impression of Change Itch specific
SCORAD	SCORing Atopic Dermatitis Index
SKINDEX	Brief Quality-of-Life Measure for Patients with Skin Diseases
SP	Substance P
VAS	Visual Analog Scale

References

1. George DT, Gilman J, Hersh J, Thorsell A, Herion D, Geyer C, Peng X, Keilbasa W, Rawlings R, Brandt JE, Gehlert DR, Tauscher JT, Hunt SP, Hommer D, Heilig M. Neurokinin 1 receptor antagonism as a possible therapy for alcoholism. Science. 2008; 319(5869):1536-9.

2. Almeida TA, Rojo J, Nieto PM, Pinto FM, Hernandez M, et al. Tachykinins and tachykinin receptors: structure and activity relationships. Current Medicinal Chemistry. 2004;11:2045-2081.

3. Hargreaves R, Ferreira JC, Hughes D, Brands J, Hale J, Mattson B, Mill S. Development of aprepitant, the first neurokinin-1 receptor antagonist for the prevention of chemotherapy-induced nausea and vomiting. Annals of the New York Academy of Sciences. 2011; 1222:40-48.

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FORWARD LOOKING STATEMENTS

Various statements in this release 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 NK-1R inhibition to provide significant benefit in the treatment of chronic pruritus in patients with atopic dermatitis; the results of Vanda's clinical development activities for tradipitant; delays in the completion of Vanda's clinical development of tradipitant; a failure of tradipitant to be demonstrably safe and effective; and other factors that are described in the "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, 2016 and quarterly report on Form 10-Q for the quarter ended June 30, 2017, which are on file with the SEC and available on the SEC's website at www.sec.gov. In addition to the risks described above and in Vanda's annual report on Form 10-K and quarterly reports on Form 10-Q, other unknown or unpredictable factors also could affect Vanda's results. 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.

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 release is provided only as of the date of this 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.

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View original content:http://www.prnewswire.com/news-releases/vandas-tradipitant-improves-itch-and-disease-severity-in-patients-with-atopic-dermatitis-300519177.html

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