Novan Provides Update on SB414 Inflammatory Skin Disease Development Program

SB414 – Nitric Oxide-Releasing Cream – Safe and Well-Tolerated in Psoriasis Phase 1b Trial

Preclinical Data with SB414 Targeting Key Inflammatory Cytokines IL-4 and IL-13 in Atopic Dermatitis
to be presented at International Investigative Dermatology Meeting

MORRISVILLE, N.C., May 15, 2018 (GLOBE NEWSWIRE) -- Novan, Inc. ("the Company" or "Novan") (NASDAQ:NOVN) today is providing an update on the SB414 nitric oxide-releasing cream product candidate and its application to two therapeutic indications: psoriasis and atopic dermatitis. As previously communicated on an investor webcast in October of 2017, the application of the Company's underlying science, as applied to inflammatory-based dermatological indications, is an important part of the Company's effort of exploring the full breadth of possibilities for its nitric oxide platform.

Novan is conducting two complementary, exploratory Phase 1b clinical trials in psoriasis and atopic dermatitis with SB414. Upon completion of both trials and analysis of associated data, the Company expects to be in a position to draw initial conclusions regarding possible paths forward for its inflammatory skin disease program, including obtaining added insights into the different mechanisms of action for each indication, and report such conclusions in the second half of 2018.

Psoriasis—Phase 1b Clinical Trial Complete

SB414 was evaluated in a Phase 1b multi-center, double-blind, randomized, vehicle-controlled trial conducted in 36 male and female patients, ages 18 to 70, with mild-to-moderate chronic plaque psoriasis. Patients were treated with SB414 6% or vehicle cream twice daily for four weeks and evaluated for safety and tolerability. At the end of the four-week treatment period, samples were collected for pharmacokinetic (PK) and pharmacodynamic (PD) analyses.

Preliminary topline results and next steps:

- SB414 was found to be safe and well-tolerated in the trial.
- The Company is continuing to analyze the PK (systemic exposure) and PD (a panel of inflammatory biomarkers) data from the trial; potential further analyses will enable the generation of additional data and associated learnings regarding patient characteristics (e.g., gender/age), disease progression (treatement-naïve, mild, moderate), co-morbidities and others.
- Complete results and analyses, as well as initial conclusions and potential next steps regarding SB414 and the inflammatory skin disease program using the underlying nitric oxide technology, will be reported following completion of the complementary atopic dermatitis trial and subsequent data generation, as previously communicated.

“The Phase 1b trial with SB414 in patients with psoriasis was our first experience with SB414 cream in the clinic, and it has shown a safe and tolerable profile similar to the profiles of SB204, SB206 and SB208,” stated Paula Brown Stafford, Novan’s Chief Development Officer and Director. “We are analyzing the PK and PD data, which together with data from the ongoing Phase 1b study in patients with atopic dermatitis, will help inform next steps for our inflammatory skin disease program.”

Atopic Dermatitis—Phase 1b Clinical Trial Fully Enrolled

A Phase 1b trial is being conducted in 48 male and female patients, ages 18 and older, with mild-to-moderate atopic dermatitis covering up to 30% body surface area at baseline. Patients are receiving two doses of SB414 cream or vehicle, applied twice daily for two weeks. As with the Company’s Phase 1b trial in psoriasis, the primary objective of this exploratory trial is to better understand SB414’s safety and tolerability, possible systemic exposure and activity against inflammatory biomarkers in patients with atopic dermatitis.

The Company is pleased to report that the trial has fully enrolled and continues to target receipt of initial topline results in the third quarter of 2018. Complete results and analyses from both the psoriasis and atopic dermatitis trials are targeted to be reported in the second half of 2018, along with potential next steps for SB414 and the inflammatory skin disease program.

Atopic Dermatitis—Preclinical Study Data to be Presented at International Investigative Dermatology Meeting

Importantly, as part of the Company's continued work around its nitric oxide platform and the platform's mechanistic application to inflammatory skin diseases, the Company will be highlighting data from preclinical studies with SB414 during a presentation at the upcoming International Investigative Dermatology meeting held May 16-19th in Orlando, Florida.

An atopic dermatitis mouse model, which had previously been used to correlate the role of *Staphylococcus aureus* in the upregulation of inflammation, demonstrated that topically applied 6% SB414 cream reduced pro-inflammatory cytokines IL-4 and IL-13 by 87% and 76%, respectively, over vehicle. The *Staphylococcus aureus* levels in the skin of SB414-treated mice were also reduced by greater than 90% over vehicle-treated mice.

"In the management of atopic dermatitis, the ability to directly target pro-inflammatory cytokines that perpetuate the disease, like IL-4 and IL-13, is key for sustained benefit," stated Emma Guttman, M.D., Ph.D., Sol and Clara Kest professor of dermatology, vice chair of research and director of the Center for Excellence in Eczema, Icahn School of Medicine at Mount Sinai Medical Center, New York. "These results generated with SB414 indicate an effect on the atopic dermatitis inflammatory pathway, as well as the bacteria that exacerbate this pathway, and lends promise to a single, nonsteroidal, dual-action topical therapy that could benefit AD patients."

About the Presentation

Abstract Number: LB1571
Title: "Effects of SB414 Cream on S. aureus and tissue cytokines in an atopic dermatitis mouse model"
Authors: S. Hollenbach, T. Nakatsuji, R. Gallo, N. Stasko
Presenter: Nathan Stasko, Ph.D.
Date and Time: Thursday, May 17, 2018, 11:45 a.m. – 1:45 p.m. Eastern Time

About Psoriasis

Psoriasis is a chronic inflammatory skin disease that affects approximately 7.5 million people in the United States.[1] The disease is characterized by an errant immune-system response that drives inflammation and thickening of the skin caused by rapid turnover of skin cells. This typically results in patches of plaques, or thick, red raised skin with silvery-

white scales.[2,3] Psoriasis can cause tremendous discomfort and can interfere with normal daily activities.[1] It has also been associated with increased incidence of a number of other diseases[1] as well as significant psychological and emotional effect, including social isolation, depression and suicide.[1,2] In fact, as many as 50% of psoriasis patients may experience depression.[1]

There is no cure for psoriasis.[3] The healthcare market has seen an increase in the introduction of systemic therapies, including biologics, to treat patients with higher disease burden, but all of the current systemic therapies are indicated only for patients with moderate-to-severe disease. For the approximately 80% of patients with mild-to-moderate psoriasis, prescription treatment options include topical corticosteroids, retinoids and vitamin D3.[1,2] None of the currently approved therapies are without side effects, and none are well-suited for chronic use.[2,3]

About Atopic Dermatitis

Atopic dermatitis, also known as atopic eczema, is the most common chronic relapsing inflammatory skin disease, affecting nearly 18 million people in the United States.[4] Stabilizing the disease and reducing the number and severity of flares are the primary goals of current treatment. The diseases is characterized by intense itching, dry skin with red papules and plaques, “weeping” clear fluid, crust and scaling. Immune cells in the deep layers of skin release inflammatory signals, causing an itchy rash. Scratching leads to defects in the skin barrier function, allowing environmental triggers, such as the bacteria *Staphylococcus aureus*, to penetrate the skin barrier and further exacerbate the condition, triggering the “itch-scratch” cycle. *S. aureus* has a proven association with atopic dermatitis. More than 90% of atopic dermatitis patients have skin that is colonized with *S. aureus*.[5,6] The density of *S. aureus* colonization has been correlated with both the severity of atopic dermatitis lesions and the degree of cutaneous inflammation. A recent study showed that the entry of *S. aureus* into the dermis triggers immune abnormalities seen in atopic dermatitis skin.[7]

Nearly eighty percent of the atopic dermatitis population suffers from mild-to-moderate disease and are treated with first-line monotherapies, however, corticosteroids and calcineruin inhibitors have side effects and are not well-suited for chronic use.[4] Recently, the first biologic treatment for atopic dermatitis targeting IL-4 and IL-13 was approved, but it is reserved for patients with moderate-to-severe disease. A topical phosphodiesterase-4

(PDE4) inhibitor was also recently approved after more than a decade of absence of therapies representing a new mechanism of action.

References

[1]American Academy of Dermatology . "Psoriasis." https://www.aad.org/media/stats/conditions/psoriasis (Nov. 15, 2016)
[2]National Institutes of Health. "Questions and Answers about Psoriasis."
[3] Vaidya T, Feldman SR, Kirk J. Patient-centered approach to biologics in the treatment of psoriasis. Journal of Nature and Science. 2015 Mar;1 (3):e53.
[4]IMS Health Disease Insights. "Atopic Dermatitis – US." June 2015.
[5]Higaki S., et al. Int J Dermatol. 1999. 38, 265-269.
[6]Gong J.Q. et al. Br J Dermatol. 2006. 155(4), 680-687.
[7]Nakatsuji T., et al. J Invest Dermatol. 2016. 136(11):2192-2200.

About Novan

Novan, Inc. is a clinical-stage biotechnology company focused on leveraging nitric oxide's natural antiviral and immunomodulatory mechanisms of action to treat dermatological and oncovirus-mediated diseases. We believe that our ability to conveniently deploy nitric oxide in a solid form, on demand and in localized formulations allows us the potential to significantly improve patient outcomes in a variety of diseases.

Forward-Looking Statements

This press release contains forward-looking statements including, but not limited to, statements related to pharmaceutical development of nitric oxide-releasing product candidates, our potential partnership opportunities, and the future prospects of our business and our product candidates. Forward-looking statements are subject to a number of risks and uncertainties that could cause actual results to differ materially from our expectations, including, but not limited to, risks and uncertainties in the clinical development process, including, among others, length, expense, ability to enroll patients, reliance on third parties, and that results of earlier research and preclinical or clinical trials may not be predictive of results, conclusions or interpretations of later research or trials and other risks and uncertainties described in our annual report filed with the SEC on Form 10-K for the twelve months ended Dec. 31, 2017, and in our subsequent filings with the SEC. These forward-looking statements speak only as of the date of this press release, and Novan disclaims any intent or obligation to update these forward-looking statements to

reflect events or circumstances after the date of such statements, except as may be required by law.

CONTACT:

(Investors)
Novan, Inc.
investors@novan.com

(Media)
Cari Green
Director, Corporate Communications and Administration
cgreen@novan.com