



Novan Announces Promising Clinical Results with SB414

August 20, 2018

- **In the recently completed Phase 1b trial for atopic dermatitis, clinical efficacy measures were highly correlated with critical and disease-relevant biomarker changes suggesting a topical nitric oxide therapeutic has the potential to realize disease modification**
- **The combination of clinical and biomarker evidence supports progressing nitric oxide-based treatments for multiple inflammatory skin diseases, including, but not limited to, atopic dermatitis, psoriasis and acne rosacea**
- **These outcomes further reinforce the potential of the properties of the nitric oxide science and underlying Novan technology platform**

MORRISVILLE, N.C., Aug. 20, 2018 (GLOBE NEWSWIRE) -- Novan, Inc. ("the Company" or "Novan") (Nasdaq:NOVN) today announced an update on the SB414 nitric oxide-releasing cream product candidate and its application to two therapeutic indications: atopic dermatitis and psoriasis. Based on results of two complementary Phase 1b clinical trials with SB414 in patients with psoriasis and atopic dermatitis, Novan intends to advance the development of SB414 as a treatment for atopic dermatitis and conduct additional exploratory trials in psoriasis and acne rosacea.

The purpose of the two randomized, double-blind, vehicle-controlled Phase 1b trials was to assess target engagement through a reduction of key inflammatory biomarkers and to evaluate the systemic exposure of SB414. The trials were also designed to measure the safety, tolerability and initial efficacy endpoints of SB414 in patients.

In the Phase 1b trial for mild-to-moderate atopic dermatitis, 48 adults were randomized to receive one of 2% SB414 cream, 6% SB414 cream, or vehicle, twice daily for two weeks. Results of this trial are shown below.

- Biomarkers from the Th2 and Th22 inflammatory pathways known to be highly relevant and indicative of atopic dermatitis, including Interleukin-13, or IL-13, IL-4R, IL-5 and IL-22, were downregulated after two weeks of treatment with SB414 2%, achieving statistically significant 10.5, 2.5, 7.1 and 7.5-fold reductions over vehicle, respectively.
- The changes in Th2 and Th22 biomarkers and clinical efficacy assessed as the percent change in Eczema Area Severity Index (EASI) scores were highly correlated in the SB414 2% group.
- Additionally, the proportion of patients achieving a greater than or equal to 3-point improvement on the pruritus (itch) numeric rating scale (NRS) after two weeks of treatment was 71% for patients treated with SB414 2% compared to 43% for vehicle.

"The biomarker analyses showed a large and significant treatment effect with SB414 2% and the direction of the change in various biomarkers was consistent," 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. "Biomarker movement typically appears before clinical efficacy. Seeing movement in Th2 cytokines (including IL-13, IL-4R and IL-5), and Th22 cytokines (including IL-22), which are strong contributors to atopic dermatitis, as well as Th17 cytokines (including IL-17A, IL-17F) in only two weeks, is encouraging."

The Phase 1b trial design for atopic dermatitis was purposefully short in duration and small in sample size and, as such, substantive clinical efficacy data was not expected to be generated. However, the Company observed that the mean changes in EASI scores were more favorable for SB414-treated patients than those on vehicle. Directional consistency in the clinical data further reinforces the strong correlation with key biomarker signals.

In the Phase 1b trial for mild-to-moderate chronic plaque psoriasis, 36 adults received SB414 6% cream or vehicle twice daily for four weeks. Analysis of the data revealed that various known biomarkers related to psoriasis were not downregulated after four weeks of treatment with SB414 6%.

Both doses of SB414 were safe as defined by no serious adverse events and SB414 2% was more tolerable with no patients discontinuing treatment in the trial due to application site reactions. SB414 at the 6% dose was not consistently effective in reducing biomarkers across both the atopic dermatitis and psoriasis trials. This lack of consistent biomarker movement could potentially be explained by the increased irritation score experienced by patients treated with SB414 6% in both trials. Additionally, SB414 6% showed detectable systemic exposure in a subset of patients, which cleared in nearly all affected patients within 12 hours.

Given the successful downregulation of key biomarkers, favorable tolerability and lack of systemic exposure with SB414 2%, Novan intends to advance the development of SB414 as a treatment for atopic dermatitis and explore the use of lower doses of SB414 in psoriasis.

"We are pleased with the findings from these two studies and have accomplished our initial goals of understanding the clinical utility and target engagement of SB414 to treat inflammatory skin diseases, as well as translating our mechanistic insights from animal models to the clinic," said Tomoko Maeda-Chubachi, M.D., Novan's Vice President of Medical Dermatology. "These favorable results from the atopic dermatitis trial and the manner in which biomarkers were affected informs our decision to move forward with future studies. We believe a larger, longer study in atopic dermatitis, further evaluation of psoriasis given the reduction of Th17 cytokines including IL-17, and exploration of nitric oxide in acne rosacea is warranted from a science, clinical and patient need point of view."

The data from the atopic dermatitis trial will be submitted for presentation by Drs. Guttman and Maeda-Chubachi at upcoming scientific and medical meetings.

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.¹ Nearly eighty percent of the atopic dermatitis population suffers from mild-to-moderate disease and are treated with first-line monotherapies, however, corticosteroids and calcineurin inhibitors have side effects and are not well-suited for chronic use.² 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.

Stabilizing the disease and reducing the number and severity of flares are the primary goals of current treatment. The disease 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. The density of *S. aureus* colonization has been correlated with both the severity of atopic dermatitis lesions and the degree of cutaneous inflammation.²

About Psoriasis

Psoriasis is a chronic inflammatory skin disease that affects approximately 7.5 million people in the United States.³ 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.^{4,5} 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 diseases³ as well as significant psychological and emotional effect, including social isolation, depression and suicide.^{3,4} In fact, as many as 50% of psoriasis patients may experience depression.³

There is no cure for psoriasis.⁵ 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.^{3,4} None of the currently approved therapies are without side effects, and none are well-suited for chronic use.^{4,5}

References

¹IMS Health Disease Insights. "Atopic Dermatitis – US." June 2015.

²Nakatsuji T., et al. *J Invest Dermatol*. 2016. 136(11):2192-2200.

³American Academy of Dermatology. "Psoriasis." <https://www.aad.org/media/stats/conditions/psoriasis> (Nov. 15, 2016)

⁴National Institutes of Health. "Questions and Answers about Psoriasis."

⁵ 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.

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.

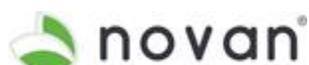
Forward Looking Statements

This press release contains forward-looking statements including, but not limited to, statements related to pharmaceutical development of nitric oxide-releasing product candidates, our intention to advance development of certain product candidates, which is subject to our ability to obtain additional financing or enter into strategic relationships to enable such development, 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 activities or additional trials; risks related to the regulatory approval process, which is lengthy, time-consuming and inherently unpredictable; risks related to the manufacture of clinical trial materials and commercial supplies of any potentially approved product candidates, including the manufacture of our NVN1000 active pharmaceutical ingredient in our primary facility; our ability to obtain substantial additional funding for the further advancement and development of our product candidates, including the SB414 anti-inflammatory program; our ability to identify and enter into strategic relationships for the further development and potential commercialization of our product candidates; and other risks and uncertainties described in our annual report filed with the SEC on Form 10-K for the twelve months ended December 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.

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