



Novan to Present Positive Phase 2 Results for SB208 Antifungal Program at Winter Clinical Dermatology Conference

Topical Nitric Oxide-Releasing Gel Shows Antifungal Activity in Tinea Pedis Infections

MORRISVILLE, N.C., Jan. 11, 2018 (GLOBE NEWSWIRE) -- Novan, Inc. ("the Company" or "Novan") (NASDAQ:NOVN) today announced that Phase 2 efficacy and safety data for SB208, a topical, silicone-based gel under development for the treatment of fungal infections of the skin and nails, such as tinea pedis, or athlete's foot, and onychomycosis, will be presented at the Winter Clinical Dermatology Conference to be held January 12th through the 17th in Maui, Hawaii.

"Onychomycosis and tinea pedis are often coexistent and persistent fungal infections, in part because there are no currently-approved topical therapies that treat both with a single product," said Dr. Leon Kircik, board-certified dermatologist, associate clinical professor of dermatology at Indiana University Medical Center in Indianapolis and Icahn School of Medicine at Mount Sinai Medical Center in New York and medical director of DermResearch, PLLC and Physicians Skin Care, PLLC. "Having a simple, effective, one-step treatment with a unique mode-of-action would be a significant advancement in the real world of treating these patients."

Recent studies suggest that the nail plate, interdigital space and surrounding tissue may serve as an overlooked reservoir of dermatophytes, perpetuating reinfection and coinfection of onychomycosis and tinea pedis.¹ In preclinical studies, Novan's nitric oxide-based drug candidate exhibited a greater than 99.9% fungal reduction of the dermatophyte *Trichophyton rubrum* in vitro in as little as four hours, and in a separate human nail penetration assay, killed greater than 90% of fungus on the underside of the nail following a single topical treatment. "The results from our Phase 2 dose ranging trial, in combination with our existing preclinical antifungal data, support the development of SB208 as a potential nitric oxide-based solution for treating patients with multiple fungal infections," said Nathan Stasko, Ph.D., President and Chief Scientific Officer of Novan.

In a Phase 2 double-blinded, randomized, vehicle-controlled, dose-ranging clinical trial, the tolerability, safety and antifungal activity of SB208 was evaluated in 222 patients with



clinical signs and symptoms of tinea pedis, or Athlete's Foot. Patients were randomized evenly to one of three active or vehicle treatment arms, applying either SB208 Gel (2%, 4% or 16%) or vehicle once-daily for two weeks, followed by a four-week post-treatment observation period.

Efficacy assessments were made on a modified intent-to-treat population (mITT) comprised of patients who had a positive baseline culture for dermatophytes such as *T. rubrum*.

- In the primary efficacy analysis of subjects with evaluable culture results, 61.3% ($p=0.209$) of patients treated with SB208 2%, 80.6% ($p=0.002$) of patients treated with SB208 4% and 74.2% ($p=0.016$) of patients treated with SB208 16% achieved negative fungal culture at day 14 versus 45.5% of patients treated with vehicle.

Mycological cure, defined as both a negative fungal culture and a negative skin scraping for the presence of fungus, was assessed at day 14 and after a four week follow up period at day 42 as secondary efficacy endpoints.

- The percentage of patients achieving mycological cure at the day 14 visit was 34.4% ($p=0.305$) of the patients treated with SB208 2%, 50.0% ($p=0.009$) of the patients treated with SB208 4% and 53.1% ($p=0.010$) of patients treated with SB208 16% versus 23.5% of patients treated with vehicle.
- At day 42, the highest mycological cure rates were observed in 58.8% of patients treated with SB208 16% ($p=0.020$ compared to vehicle).

Clinical signs and symptoms of tinea pedis were also evaluated on a four-point scale ranging from none to severe at each assessment timepoint. Signs and symptoms included erythema, scaling, maceration, cracking, pruritus and burning/stinging. Efficacy measures of clinical cure were defined as a sum of total signs/symptoms severity score of no more than two with no individual symptom severity score greater than one. The clinical cure response rates were greatest at day 42, 4 weeks after treatment, and the two highest SB208 dose groups (4 and 16%) were approximately two times higher than the response rate for vehicle and SB208 2%.

- The percentage of patients achieving clinical cure at day 42 was 14.3% of the patients treated with SB208 2%, 29.7% of the patients treated with SB208 4%, and 25.0% of patients treated with SB208 16% versus 14.3% of patients treated with vehicle.



The overall incidence of adverse events was low (9 subjects or 4%) and similar in all groups. None of the treatment emergent adverse events were determined to be related to the study medication, and no patients discontinued treatment or dropped out of the study due to an adverse event.

Based on the positive data generated in this SB208 Phase 2 dose-ranging trial, Novan intends to evaluate potential partnerships to advance the antifungal candidate into later stages of development.

About Onychomycosis

Onychomycosis is a chronic fungal infection of the nails that affects approximately 40 million Americans and accounts for one-third of cutaneous fungal infections. The prevalence of disease increases with age, and more than 50% of patients are 70 years or older. The infection, caused by dermatophytes such as *Trichophyton rubrum*, often results in painful thickening and deformation of the nail and sometimes the separation of the nail plate from the nail bed, leading to an inability of the nail to perform its natural protective function. Oral therapies used to treat the infection are associated with severe side effects, and topical therapies have modest efficacy profiles with complete cure rates of less than 20%.

About Tinea Pedis

Tinea pedis, often referred to as Athlete's Foot, is a common fungal infection of the feet, affecting approximately 75 million Americans. *Trichophyton rubrum* is the most prominent dermatophyte in tinea pedis and also a causative pathogen in onychomycosis.

Approximately one-third of onychomycosis patients also suffer from tinea pedis. Topical treatments are the first-line therapy for tinea pedis, while oral antifungals are prescribed when the infection is severe, or the use of topical antifungals is not feasible. Currently, there is no approved single topical therapeutic agent that provides for the simultaneous treatment of the nail plate, bed, and surrounding cutaneous tissue.

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; the lengthy and unpredictable nature of the U.S. Food and Drug Administration's drug approval process; whether we will be able to enter into strategic arrangements or obtain adequate funding to support our operations and initiatives on acceptable terms, or at all, 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, 2016, 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.

References

¹Lipner SR, Scher RK. 2015. Management of onychomycosis and co-existing tinea pedis. *J Drugs Dermatol* 14(5):492-94.

²Markinson B, Caldwell B. 2015. Efinaconazole topical solution, 10% efficacy in patients with onychomycosis and coexisting tinea pedis. *J Am Podiatr Med Assoc* 105(5):407-11.

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