

## **Novan Announces Successful Phase 2b Clinical Trial Results with SB204 for the Treatment of Acne Vulgaris**

### **First-in-Class Nitric Oxide-Based Acne Therapy Set to Begin Phase 3 Trials in Early 2016**

**DURHAM, N.C. — September 29, 2015** – Novan Therapeutics announced today positive Phase 2b study results of its [topical nitric oxide drug candidate SB204](#) for the treatment of acne vulgaris, achieving the company’s program goals. The Phase 2b study demonstrated statistically significant reductions in the percent change of non-inflammatory (white heads and black heads) and inflammatory (larger red bumps and pustules) lesions at Week 12 with all doses of SB204 compared to Vehicle. SB204 demonstrated excellent cutaneous tolerability with no treatment-related serious adverse events in over 400 dosed subjects to date. Across the entire Phase 2 development program, less than 1% of enrolled subjects treated with active or vehicle were discontinued due to local application site adverse events.

“These study results reproduce our [Phase 2a trial](#) which showed a similar separation between active drug and vehicle,” said Nathan Stasko, Ph.D., Novan’s president. “Replicating a 20% differential between SB204 and Vehicle in percent lesion reduction gives us great confidence in moving into the Phase 3 program.”

Based on these results and having completed an End-of-Phase 2 meeting with the FDA, Novan plans to initiate two pivotal Phase 3 trials with SB204 once daily in the first quarter of 2016, targeting enrollment of 1,300 subjects per trial.

“The magnitude of separation from Vehicle we are observing with a once daily monotherapy is comparable to the separation on acne lesions observed for commercially available combination products utilizing two active agents. We engineered a new chemical entity that uses nitric oxide to target multiple aspects of acne pathology, including the elimination of *P. acnes* without the use of an antibiotic, reduction of sebum excretion, and decrease of inflammation,” added Dr. Stasko.

Steven Feldman, M.D., Ph.D. at the Department of Dermatology, Wake Forest Baptist Medical Center commented, “Tolerability, adherence, and efficacy have a direct linkage. Physicians and patients need new treatment options with improved side effect profiles. Novan’s SB204 product has shown promising tolerability and an impressive level of efficacy for a monotherapy that may limit resistance to antibiotics.”

Oral and topical antibiotics, including clindamycin, have been a mainstay for treating acne but long-term use is contributing to the development of antimicrobial resistant bacteria. Clindamycin-resistant Group B Streptococcus is listed on the Center for Disease Control’s [list of the top 18 drug-resistant threats](#) to the United States, published in 2013. The American Academy of Dermatology is expected to review and update guidelines of care for the management of acne vulgaris, [with a focus on the use of antibiotics](#), later this year.

### **SB204 Phase 2 Clinical Program Results**

#### Phase 2b (NI-AC202)

In Novan’s double-blind, vehicle-controlled Phase 2 study conducted across 20 sites in the United States, 213 subjects were randomized to five treatment arms: SB204 2% twice daily,

SB204 4% once daily, SB204 4% twice daily and Vehicle once or twice daily and treated for up to 12 weeks. Data from Vehicle treated subjects were pooled for analysis. All doses of SB204 showed statistically significant reductions in the percent change of non-inflammatory and inflammatory lesions compared to Vehicle at the 12-week endpoint (intent-to-treat population). At the end of treatment, the only dose group to be statistically significant in both absolute change and percent change for both lesion types was the SB204 4% once daily treatment arm. The absolute change from baseline in inflammatory lesions was -11.3 (42%) for 4% once daily and -5.8 (19%) for Vehicle ( $p=0.004$ ) and the absolute change from baseline in non-inflammatory lesions was -14.1 (37%) for 4% once daily and -7.6 (17%) for Vehicle ( $p=0.032$ ).

In a time-to-event analysis, the 4% once daily treatment demonstrated a time-to-median improvement of 4.1 weeks compared to 11.6 weeks for Vehicle ( $p=0.014$  as defined by a 35% reduction in inflammatory lesions). A 6% difference between the pooled SB204-treated subjects and Vehicle-treated subjects was observed in the Investigator Global Assessment (IGA) endpoint. While not statistically significant, this difference in IGA enables the power calculations for future Phase 3 pivotal studies with a 95% confidence interval. At the end of 12 weeks of treatment, <5% of the subjects had a cutaneous tolerability score of 'moderate' for any of the local tolerability assessments (erythema, dryness, scaling, itching, burning/stinging) with zero reported subjects having any severe local application site reactions.

#### Phase 2a (NI-AC201)

In Novan's first Phase 2, double-blind, vehicle-controlled, parallel-group, 3-arm study conducted at four sites in Latin America, 153 subjects were randomized to twice daily treatment with SB204 1%, SB204 4%, or Vehicle in a 1:1:1 ratio and treated for 12 weeks. At four weeks, the 4% dose of SB204 demonstrated a statistically significant reduction in both non-inflammatory and inflammatory lesions compared to Vehicle ( $p \leq 0.05$ , intent-to-treat population). Statistically significant reductions were observed in the primary and secondary endpoints for both lesion types at the 12 week time point. The absolute change from baseline in inflammatory lesions was -15.5 (54%) for 4% twice daily and -9.3 (35%) for Vehicle ( $p=0.018$ ) and the absolute change from baseline in non-inflammatory lesions was -11 (26%) for 4% twice daily and -0.3 (1%) for Vehicle ( $p=0.031$ ). Clinical reductions in sebum excretion were observed with a mean reduction of approximately 80% in SB204-treated subjects as compared to Vehicle ( $n=70$  subjects, *ns*). There were no statistically significant differences in the dichotomized IGA scores of 'success' (score of "clear/almost clear" and minimum two grade change between baseline and Week 12) between Vehicle and SB204 1% or SB204 4% treatment groups.

## **About Novan, Inc.**

Novan is a privately-held, clinical stage biotechnology company advancing therapies for skin diseases using drugable nitric oxide. Nitric oxide, one of the most studied molecules in human physiology, has been shown to exhibit broad anti-microbial activity and to promote vasodilation, regulate inflammation, stimulate tissue repair, and eradicate cancer cells. Novan's patented Nitricil™ technology overcomes the previous delivery issues with nitric oxide by stably storing the gaseous species as a solid that can be transformed into targeted therapeutics.

This press release contains forward-looking statements involving risks and uncertainties, both known and unknown, that may cause actual results to differ materially from those indicated. Actual results may differ materially due to a number of factors, including, but not limited to, risks associated with pharmaceutical development, clinical trials that may not proceed as intended or produce the results expected, clinical trials that cost more, are less effective and take longer to complete than expected, raw materials and drug supply, changes in regulatory requirements, competition, and financing.

To learn more about Novan Therapeutics, please visit [www.novantherapeutics.com](http://www.novantherapeutics.com).

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