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Novan seeks to unleash power of nitric oxide in 'tunable' drugs

By Marie Powers, Staff Writer

For nearly two decades, scientists have appreciated the healing power of nitric oxide (NO), a free radical that garnered researchers at three U.S. institutions the 1998 Nobel Prize in Physiology or Medicine for their discoveries involving NO as a signaling molecule in the cardiovascular system. Despite its promise, NO's potential has been limited by the fact that the substance is gaseous and highly reactive, confounding the ability of drug developers to store and deliver it safely in the right amount, to the right location and at the right time.

Novan Therapeutics Inc. believes it has created the magic bullet to overcome those problems. The company's core technologies solve delivery issues by storing the gaseous species as an engineered molecule that allows for the timed release of NO in short- or long-term applications. By storing nitric oxide as part of an engineered molecule, the technology can be controlled to "tune" the level of NO storage, the rate of NO release and the molecule size to target NO delivery. The result is a stabilized form of NO that can be used as a drug across a variety of indications, beginning with topical use in acne vulgaris, atopic dermatitis and common warts.

Novan was initially formed to pursue a device application, but in 2010 the company turned its attention to drug development, using core technology licensed from the University of North Carolina at Chapel Hill, according to Nathan Stasko, co-founder and president of the Durham, N.C.-based firm. The company subsequently in-licensed additional complementary technology, amassing an intellectual property portfolio that comprises more than 70 patents and applications.

The key to the company's technology is its ability to tailor the formulation of NO to each particular application. Novan can engineer the release profile of NO-releasing macromolecules to provide a rapid burst, a sustained release and anything in between, creating NO therapeutics with a release half-life ranging from seconds to days.

"Our macromolecular delivery mechanism is the differentiator," Stasko told *BioWorld Today*.

'WE DON'T PLAN TO BE A ONE-HIT WONDER'

Novan is focusing first on dermatology applications because a large body of evidence has demonstrated NO's role in tamping down inflammation and killing even the most virulent, drug-resistant pathogens.

"Nitric oxide is part of the body's natural immune response," Stasko said. "We're taking a cue from the body."

Last year, Novan reported findings from a phase I trial in 30 volunteers showing that lead candidate SB204 reduced skin colonization by *Propionibacterium acnes*. The results suggested the candidate was effective against acne, particularly in combination with previous findings related to sebum production, with several subjects experiencing greater than 90 percent reduction of *P. acnes*. The study also showed a statistically significant difference ($p < 0.05$) between the active arm and vehicle after just two weeks.

Novan followed that study with a 12-week, multicenter, double-blind, randomized, vehicle-controlled, parallel-group, dose-ranging phase II trial evaluating the safety, tolerability and efficacy of SB204 gel in approximately 150 subjects with acne vulgaris. Novan plans to disclose the findings next month at the annual meeting of the American Academy of Dermatology in Denver but, suffice to say, the company is excited about the data.

Acne is an indication begging for new molecular entities, Stasko maintained. Most products on the market today are generics, reformulations or drug combinations.

"Most dermatologists will tell you that they're starving for new mechanisms of action," he said. "The really big unmet need in acne is the ability to reduce sebum, and we believe our drug has shown the ability to do that."

Stasko also is confident that clinical validation from the acne program will translate to other therapeutic areas, with wound care – infection, chronic wounds and burns – next on the agenda.

"Our goal as a company is to generate a pipeline of drugs based on nitric oxide," he said. "We don't plan to be a one-hit wonder."

Acne, alone, is a potential $3 billion market in the U.S., according to Stasko. From a product development standpoint, the aesthetics space also is hot, giving the company the potential to generate sustainable revenue to expand its development programs.

With that in mind, Novan had something of a coming-out party last month, when Stasko was a presenter at

the inaugural Dermatology Summit in San Francisco, held in conjunction with the 32nd Annual J.P. Morgan Healthcare Conference. The summit attracted keynoters from industry powerhouses such as Galderma SA, Merz Pharma GmbH & Co. KgaA, Glaxosmithkline plc unit Stiefel Laboratories Inc., Kythera Biopharmaceuticals Inc. and Allergan Inc., as well as top academic researchers and investment firms.

"It was an exciting time for us, because we had just come off the phase II trial in acne, and this was Novan's first step toward becoming a player in the derma industry," Stasko said.

His goal in San Francisco was "to meet with enough parties on both sides of the house" to explore the company's options in partnering as well as outside financing.

To date, Novan has raised $20 million in private funding from high net worth individuals and captured more than $15 million in grant monies from a variety of federal agencies, including the National Institutes of Health, National Science Foundation, Department of Defense and Biomedical Advanced Research and Development Authority.

The company now is talking with private equity firms, investment banks and venture funds and beginning to explore strategic collaborations with potential partners. Stasko's goal over the next 12 to 18 months is to complete at least three proof-of-concept studies in dermatology applications, which are "within striking distance," he said. The company also is receptive to collaboration in larger indications, such as oncology or cardiovascular disease, that would require much larger trials.

"The breadth of nitric oxide is so large that we're not going to be able to develop it alone," Stasko acknowledged. "To access all of the potential applications for all the patients who could benefit is going to require collaborations of one form or another." //