



Results from Positive Phase 2 Study of NovaDigm Therapeutics' NDV-3A Vaccine Against *Candida* Published in *Clinical Infectious Diseases*

- In First Positive Efficacy Study for an Antifungal Vaccine, NDV-3A Established Efficacy in Patients with Recurrent Vulvovaginal Candidiasis -

BOSTON – April 25, 2018 – [NovaDigm Therapeutics](#), a company developing innovative immunotherapeutics and preventative vaccines for fungal and bacterial infections, today announced the publication of data from a Phase 2a study of its NDV-3A vaccine program in the journal *Clinical Infectious Diseases*. The data demonstrate that a single dose of NDV-3A with alum adjuvant was safe, well-tolerated, immunogenic and efficacious, leading to reduced recurrences of vaginitis in patients with recurrent vulvovaginal candidiasis (RVVC). NDV-3A is the company's lead development candidate to potentially treat or prevent diseases caused by fungal and bacterial pathogens, including antimicrobial-resistant strains.

The article, titled "[A Fungal Immunotherapeutic Vaccine \(NDV-3A\) for Treatment of Recurrent Vulvovaginal Candidiasis – A Phase 2 Randomized, Double-Blind, Placebo-Controlled Trials](#)," was published online in the journal *Clinical Infectious Diseases*¹. The article was published with a concurrent editorial entitled, "[A Therapeutic Vaccine for Recurrent Vulvovaginal Candidiasis](#)," by Arturo Casadevall, M.D., M.S., Ph.D., Chair, Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health and Liise-anne Pirofski, M.D., Chief, Division of Infectious Diseases, Department of Medicine, Albert Einstein College of Medicine².

"There is a growing need for vaccines that can prevent or treat conditions caused by *Candida* species, such as *Candida albicans*, the major causative agent of RVVC," commented John Edwards, M.D., first author of the study, Emeritus Chief, Division of Infectious Disease at Harbor-UCLA Medical Center and a scientific founder of NovaDigm. "The positive results in patients with RVVC represent the first demonstration of efficacy for any antifungal vaccine. These results encourage further development of NDV-3A against life-threatening invasive *Candida* infections, including those by the recently emerging, highly drug-resistant *Candida auris*."

Nine million women in the United States (11%) report having recurrent yeast infections, with approximately seven million (9%) experiencing RVVC, which has been defined as having three or more episodes per year. Approximately 90% of patients report onset of RVVC prior to the age of 40 years³. Many of these women experience frequent episodes of pain and discomfort, high rates of depression and a reduced overall quality of life⁴. While current therapies are effective at controlling acute infections, they do not control recurrences without chronic antifungal suppression, which is not widely used due to potential adverse events.

"Women who have recurrent vulvovaginal candidiasis have limited options to maintain control of this chronic condition, which can have a significant impact on their health and overall quality of life," said Paul Nyirjesy, M.D., Professor of Obstetrics and Gynecology and of Medicine at Drexel University College of Medicine, who was a principal investigator in the Phase 2a study. "The results of this trial demonstrate

increases in recurrence-free time out to 12 months for younger women based on patient symptom scores following a single dose of NDV-3A. This finding represents a potential breakthrough for an immunotherapeutic approach to treating these patients.”

Top line results [reported in August 2016](#) show the study of 188 patients met its primary endpoint of safety and tolerability. There were no significant differences between NDV-3A and placebo for injection site reactions and systemic reactions of grade 3 or greater. A single dose of NDV-3A generated rapid and robust immune responses. Exploratory efficacy measures based on patient-reported symptom scores showed a higher proportion of patients in the NDV-3A group with no recurrences at the 12-month follow-up period compared to the placebo group ($p=0.10$). Younger patients showed higher efficacy rates. In patients under 40 years of age (77% of the study population), 42% of NDV-3A recipients were recurrence-free at 12 months post-vaccination compared to 22% of placebo recipients ($p=0.03$). Patients in this age group receiving NDV-3A also showed a doubling in median time to first recurrence (210 days) compared to placebo recipients (105 days).

About the NDV-3A Phase 2a Trial

The Phase 2a trial was a multi-center, double-blind, randomized, placebo-controlled study evaluating the safety, tolerability, immunogenicity and efficacy of NDV-3A. The study enrolled 188 patients over 20 US study sites. Patients were assigned one dose of either 300 μ g NDV-3A immunotherapy or a placebo. The primary objective of the study was to assess the safety and tolerability of a single, intramuscular dose of NDV-3A, as compared to placebo, in patients with at least three episodes of VVC in the past 12 months. Secondary objectives included assessments of humoral and cellular immune responses and various measures of efficacy in reducing the frequency and/or severity of recurrences over a 12-month period. A summary of the study can be found on the United States National Institutes of Health clinicaltrials.gov website (Identifier NCT01926028).

About the NDV-3A Development Program

NDV-3A is being developed as an immunotherapy and as a preventative vaccine for infections caused by several species of the fungus *Candida*, including *Candida albicans* and multidrug-resistant *Candida auris*, as well as the bacterium *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus* (MRSA). NDV-3A contains a recombinant form of the *Candida albicans* agglutinin-like sequence 3 (Als3) surface protein, which facilitates *Candida* adherence to and invasion of human endothelial cells. Als3 has been shown to have strong structural homology to surface proteins responsible for adherence of *S. aureus* to human endothelial cells. This finding helps to explain why NDV-3A is the first vaccine candidate to demonstrate “cross-kingdom” protection against both fungal and bacterial pathogens in preclinical studies. These studies showed that NDV-3A confers significant protection compared to placebo following bloodstream or mucocutaneous challenge with highly virulent doses of several species of *Candida* or several strains of *Staphylococcus aureus*, including MRSA strains. Two Phase 1 studies involving 200 healthy adults suggested that the vaccine is well-tolerated, safe, and induces rapid antibody and T-cell responses after a single dose, with or without alum adjuvant. A Phase 2 efficacy study of NDV-3A versus placebo in 188 patients with recurrent vulvovaginal candidiasis (RVVC) demonstrated that a single dose of NDV-3A resulted in an increase in the recurrence-free rate out to 12 months and extended the time to first recurrence for those that had a recurrence. This development program was based on research in the laboratories of NovaDigm’s scientific founders at the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center. The work was supported in part by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (Grant Numbers AI19990, AI063382 and AI071554) and by the Department of the Army (Award Numbers JW81XWH-10-2-0035, W81XWH-11-1-0686 and W81XWH-16-C-0125).

About NovaDigm

NovaDigm is developing innovative immunotherapeutic and preventative vaccines to protect patients from fungal and bacterial diseases, which can be recurrent, drug-resistant and in some cases, life-threatening. NovaDigm's lead development candidate, NDV-3A, is the first vaccine to demonstrate preclinical efficacy in reducing the severity of disease caused by both fungal and bacterial pathogens. NDV-3A is in Phase 2 clinical development for recurrent vulvovaginal candidiasis (RVVC) with follow-on indications planned for diseases associated with *Candida* and *Staphylococcus aureus* infections. www.novadigmtherapeutics.com

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³ Unpublished data from 2011 L.E.K. Consulting study of RVVC patients

⁴ Aballéa et al. Health and Quality of Life Outcomes 2013, 11:169