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NovaDigm Therapeutics Strengthens *Candida* Vaccine Portfolio with Three New Antigens via Series of Rights Acquisitions

GRAND FORKS, ND – June 10, 2014 – NovaDigm Therapeutics, a company developing innovative vaccines for fungal and bacterial infections, today announced that it has acquired the rights, in four separate transactions, to three well-studied *Candida* vaccine antigens, significantly bolstering the Company's *Candida* vaccine pipeline. These three antigens are in addition to the Company's agglutinin-like sequence 3 (Als3) antigen used in NDV-3, NovaDigm's lead vaccine being evaluated in an on-going Phase 1b/2a study.[1] NovaDigm now has four of the five most widely studied *Candida* antigens, and two of those have successfully completed Phase 1 studies.

The three antigens acquired are hyphally-regulated protein 1 (Hyr1), secreted aspartyl proteinase 2 (Sap2) and a β-mannan conjugate. Hyr1 was licensed from the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center. The use of recombinant Hyr1 as a protective antigen was discovered by NovaDigm's founding scientists, led by John E. Edwards, Jr., MD, Chair of the Division of Infectious Diseases.[2,3] Rights to Sap2 were acquired from Pevion, a Swiss biotech company, and Istituto Superiore di Sanità in Rome (Italian National Health Institute, ISS). Recombinant Sap2 antigen was developed by a team led by Professor Antonio Cassone, MD, formerly of ISS and currently at the Center of Genomics, Genetics and Biology of the University of Perugia.[4] Rights to the β-mannan trisaccharide conjugate were acquired from three leading academic researchers: David Bundle, PhD, Professor of Chemistry, the Raymond U. Lemieux Chair in Carbohydrate Chemistry, and a Distinguished University Professor at the University of Alberta, Jim E. Cutler, PhD, Professor (Retired), Pediatrics and Microbiology, Immunology & Parasitology, Louisiana State University School of Medicine and Mark Nitz, PhD, Professor of Chemistry, University of Toronto.[5]

"These acquisitions solidify NovaDigm as the leader in *Candida* vaccine development," said Timothy Cooke, Ph.D., NovaDigm's Chief Executive Officer. "As we look to expand beyond the recurrent vulvovaginal candidiasis indication, a multi-antigen vaccine may provide the best protection against invasive infections, and NovaDigm is now well-positioned to develop such a vaccine."

Candida species contain a range of factors that facilitate tissue invasion by enabling the fungus to evade, modulate or exacerbate the host's immune system. Thus, a multi-antigen vaccine approach could significantly weaken the ability of *Candida* to escape from the body's immune system and provide a more effective vaccine.

Hyr1 is a component of the *Candida* cell wall that inhibits the innate immune system's ability to kill *Candida*. In preclinical studies, an Hyr1 vaccine conferred protection from systemic candidiasis in murine

models by producing antibodies that reversed the inhibition of the immune system. Sap2 degrades essential components of the immune response and contributes to inflammation. A Phase 1 study of a Sap2-based vaccine conducted by Pevion demonstrated favorable safety and immunogenicity, inducing production of anti-Sap2 antibodies which are thought to neutralize Sap2's involvement in immune evasion and inhibit inflammatory responses. β-mannan is a key outer cell wall component of *Candida,* which may be involved in adhesion to host cells. Vaccines based on the conjugation of β-mannan to a protein carrier have demonstrated protection against both systemic and vaginal *Candida* infections in numerous preclinical studies.

NovaDigm's NDV-3 vaccine is currently in a Phase 1b/2a clinical study for the prevention of recurrent vulvovaginal candidiasis. This vaccine contains the Als3 antigen, which facilitates *Candida* adherence to and invasion of human endothelial cells.

NDV-3 Development Program

NDV-3 is a vaccine candidate containing a recombinant form of the *Candida albicans* surface protein Als3, which facilitates *Candida* adherence to and invasion of human endothelial cells. This vaccine was developed as a result of research in the labs of NovaDigm's scientific founders at the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center demonstrating that several members of the Als family of proteins induce protective immunity in preclinical models. NDV-3 is the first vaccine to demonstrate protective efficacy against both fungal and bacterial pathogens. Preclinical studies have shown that NDV-3 confers a high survival rate following a systemic challenge with highly virulent doses of one of several species of *Candida* or against one of several strains of *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus* (MRSA). NDV-3 also reduces fungal burden in mice following an oropharyngeal or intravaginal challenge. Two Phase 1 studies involving 200 healthy adults have indicated that NDV-3 is safe, well-tolerated and induces rapid antibody and T-cell responses after a single dose, with or without alum adjuvant. This 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, W23RYX-11-08-N602, W81XWH-08-1-0151 and W81XWH-11-1-0686).

About NovaDigm

NovaDigm is developing innovative vaccines to protect patients from fungal and bacterial infections, which can be recurrent, drug-resistant and in some cases, life-threatening. The Company's founding scientists from the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center (LA BioMed) are recognized leaders in the field of infectious disease and the emerging threat of "superbugs". Their work has been largely funded by the National Institutes of Health National Institute of Allergy and Infectious Diseases (NIH NIAID). NovaDigm's lead product candidates target *Candida*, a fungal pathogen, and *Staphylococcus aureus*, including MRSA. Based in North Dakota with additional research activities at LA BioMed, NovaDigm has received funding from Domain Associates, a leading U.S. health care venture capital firm and RusnanoMedInvest (RMI), a Russian venture capital firm. The company also collaborates with multiple government agencies.

References

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