Results from Positive Phase 1 Study of NovaDigm Therapeutics' NDV-3 Vaccine for *Candida* and *Staph* Infections Published in *Vaccine*

GRAND FORKS, N.D. – December 13, 2012 – NovaDigm Therapeutics, a company developing innovative vaccines for fungal and bacterial infections, today announced the publication of data from its first-in-human Phase 1 study of its NDV-3 vaccine program in the journal *Vaccine.* The data demonstrate that a single dose of NDV-3 with alum adjuvant was safe, well-tolerated and induced strong antibody and T-cell immune responses in healthy adults.

NDV-3 is a vaccine being developed for the treatment and prevention of infections caused by the fungus *Candida* and the bacterium *Staphylococcus aureus* (including methicillin-resistant *S. aureus*, or MRSA). NDV-3 is the first vaccine to demonstrate preclinical "cross-kingdom" protective efficacy against both fungal and bacterial pathogens.

"The publication of this positive data provides further validation for NovaDigm as we prepare to begin a Phase 2 efficacy study with an optimized vaccine formulation in the first half of 2013," said Timothy Cooke, Ph.D., NovaDigm's Chief Executive Officer. "We are encouraged that NDV-3 was shown to be safe and well-tolerated, with a very promising immunogenicity profile, in two Phase 1 studies. We are confident that it can play an important role in treating community- and hospital- acquired infections caused by these pathogens, which represent significant medical needs and large commercial potential."

"There is a great need for vaccines that can safely treat the wide array of infections caused by both *Candida* and *Staph aureus*," commented John Hennessey, Ph.D., corresponding author of the study and Vice President of Research & Development at NovaDigm. "In addition to the rapid antibody responses following a single dose, there were also substantial T-cell responses. These included responses to Th1 and Th17 T-cells, which are believed to be important for protection against both *Candida* and *Staph aureus*. This study is also the first to demonstrate vaccine-induced Th17 responses in humans."

The objectives of this first-in-human Phase 1 clinical trial were to evaluate the safety, tolerability and immunogenicity of NDV-3 at two different antigen levels compared to a saline placebo. Forty healthy, adult subjects were randomized to receive NDV-3 containing either 30 µg or 300 µg of the Als3 antigen with alum adjuvant or placebo. The trial data published in *Vaccine* indicated that NDV-3 was safe and well-tolerated after one or two doses, with the most common adverse event being injection site pain that was typically mild and lasted 1 to 2 days after vaccination.

Both dose levels resulted in 100% seroconversion for both serum immunoglobulin G (IgG) and serum immunoglobulin A1 (IgA1) antibodies by day 14, with greater than 50% seroconversion by day seven in

the higher dose group. The geomean fold rise in IgG and IgA1 antibody titers by day 14 post-vaccination for the higher dose group were 65- and 45-fold, respectively. Geomean IgG and IgA1 titers over the course of 28 days were significantly greater in the 300 µg dose level compared to the 30 µg dose level. Results of the study showed that the majority of subjects that received NDV-3 demonstrated significant Als3-stimulated production of the cytokines IL-17A and IFN-γ between seven and 28 days post-vaccination relative to subjects receiving placebo.

The article, titled "NDV-3, a recombinant alum-adjuvanted vaccine for *Candida* and *Staphylococcus aureus* is safe and immunogenic in healthy adults," was published in the current print issue of the journal *Vaccine (Volume 30, Issue 52,* December 14, 2012*).* The study's authors were: Clint S. Schmidt, C. Jo White, Ashraf S. Ibrahim, Scott G. Filler, Yue Fu, Michael R. Yeaman, John E. Edwards Jr. and John P. Hennessey Jr.

Top-line results reported in May 2012 from a second Phase 1 trial in 160 volunteers showed that single doses of three different formulations and two routes of administration of NDV-3 were safe, well-tolerated and highly immunogenic. The Company believes the two Phase 1 studies provide a strong foundation for further clinical development. NovaDigm is preparing to initiate a Phase 2 efficacy trial in 2013 in women with chronic vaginal *Candida* (yeast) infections.

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 agglutinin-like sequence (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 challenge with highly virulent doses of one of several species of *Candida* or against one of several strains of *S. aureus*, including methicillin-resistant *S. aureus* (MRSA). Preclinical models also show that NDV-3 reduces fungal burden following sub-lethal challenge with one of several species of *Candida*. 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 and W81XWH-11-1-0686).

Medical Need

Candida is the fungal pathogen responsible for vaginal yeast infections and the oral infection known as thrush. These mucosal candidal infections are common and can be persistent in some patients, causing recurrent disease several times per year. Most notable in this respect is recurrent vaginal yeast infections (vulvovaginal candidiasis), which impacts 5–8% of women in the US and Europe. *Candida* is

also the third most common cause of nosocomial bloodstream infections. The incidence of systemic candidiasis in the United States is at least 20 per 100,000 people, or over 60,000 infections per year, of which approximately 40% (24,000) are lethal despite antifungal treatment.

Historically, *S. aureus* was predominantly the cause of invasive infections occurring among individuals with immune deficiencies, or those in hospital settings. However, an urgent concern is the recent explosion of drug-resistant *S. aureus* infections among young and otherwise healthy individuals in the community. *S. aureus* is now a common cause of skin infections and the Centers for Disease Control estimates that 12 million physician visits annually are due to suspected *S. aureus* or MRSA skin infections. In 2008, there were an estimated 90,000 cases of invasive MRSA in the U.S., leading to 15,000 deaths (17% mortality).

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 health care venture capital firm, and collaborates with multiple government agencies. www.novadigmtherapeutics.com

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