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Dynavax Peanut Immunotherapy Inhibits Allergic Response in Preclinical Studies

BERKELEY, Calif., Nov 15, 2004 /PRNewswire-FirstCall via COMTEX/ -- Dynavax Technologies (Nasdaq: DVAX) presented data from preclinical models showing that the company's immunostimulatory sequence (ISS)-based peanut immunotherapy demonstrated potent inhibition of harmful allergic responses and induction of therapeutic immune responses to peanut allergen. The data suggest that Dynavax' peanut allergy product candidate, which consists of ISS linked to the peanut allergen, Ara h 2, has the potential to be a safe and attractive candidate for therapy in peanut allergic subjects. There are currently no products available that prevent peanut allergy. In vivo testing of peanut immunotherapy products poses the risk of anaphylaxis, and most research has been done in animal models or in vitro. Approximately 3 million Americans have peanut or tree nut allergies.

The data showed that ISS linked to Ara h 2 administered to non-sensitized mice resulted in inhibition of immunoglobulin G1 (IgG1) and interleukin-5 (IL-5), mediators associated with the harmful Th2 pathway that causes allergic response, and induction of IgG2a and Interferon gamma (IFNg), mediators associated with the protective Th1 immune response pathway. In vitro data showed that linking Ara h 2 to ISS reduced histamine release from blood cells from peanut allergic subjects and inhibited binding to IgE, findings that correlate with inhibition of allergic response. These results are consistent with the mechanism of action of ISS in reprogramming the immune system via the stimulation of the Th1 pathway and suppression of the Th2 pathway, and suggest that ISS linked to Ara h 2 has potential utility as a peanut allergy therapeutic.

"We believe that our ISS-based peanut allergy immunotherapeutic addresses the major challenge in treating this deadly allergy, namely, the ability to mask presentation of the allergen and promote a Th1 response, thus effectively transforming the allergen into a drug," said Dino Dina, MD, president and chief executive officer of Dynavax. "As these preclinical data suggest, by using ISS to block recognition of the Ara h 2 allergen by IgE and prevent subsequent histamine release, it may be possible to reprogram the immune response without inducing an allergic reaction. In addition, we believe the resulting creation of Th1 memory cells may provide long-term protection against an allergic response due to accidental exposure to peanuts. Our hope is to advance this promising program toward initiating a clinical study in the near future."

The data were presented at the annual meeting of the American College of Allergy, Asthma and Immunology, in a poster entitled, "Immunogenicity and Allergenicity of Ara h 2 Linked to Immunostimulatory DNA."

Study Results

In this study, ISS was linked to the Ara h 2 protein in two ratios: peanut ISS conjugate (PIC) consists of an average of two ISS linkages, and heavy peanut ISS conjugate (HPIC) consists of an average of four ISS linkages. Immunogenicity, or the ability to induce an immune response, was tested by administering PIC, HPIC or Ara h 2 to non-sensitized mice (two immunizations of 5 micrograms). Animals immunized with PIC showed significantly enhanced IgG2a responses and strong IFNg responses, indicative of Th1-type responses, while mice immunized with Ara h 2 elicited predominantly IgG1 and IL-5 responses, indicative of a Th2-type response. HPIC immunized mice elicited little antibody response, possibly due to B-cell epitope blockage, but did induce IFNg responses.

Allergenicity, or the ability to induce an allergic response, was also tested in a histamine release assay using blood cells from peanut allergic donors. In cells treated with low levels of Ara h 2 (0.01 nanograms per milliliter), histamine release was detected. A 10-fold higher concentration of PIC (0.1 nanograms per milliliter) was required to detect histamine release. At HPIC concentrations up to 1000-fold higher (10 nanograms per milliliter), histamine release was undetectable. A similar trend was shown in an IgE binding competition assay. The results suggest that antigen-ISS vaccines may be safe and attractive candidates for therapy in allergic subjects.

About ISS

ISS are short synthetic DNA molecules that stimulate a Th1 immune response while suppressing Th2 immune responses. ISS contain particular sequences that activate the innate immune system. ISS are recognized by a specialized subset of dendritic cells containing a unique receptor called Toll-Like Receptor 9, or TLR-9. The interaction of TLR-9 with ISS triggers the biological events that lead to the suppression of the Th2 immune response and the enhancement of the Th1 immune response. ISS influence helper T cell responses in a targeted and highly specific way by redirecting the response of only those T cells involved in a given disease. ISS, in conjunction with an allergen or antigen, establish populations of memory Th1 cells, allowing the immune system to respond appropriately to each future encounter with a specific pathogen or allergen, leading to long-lasting therapeutic effects.

About Dynavax

Dynavax Technologies Corporation discovers, develops, and intends to commercialize innovative products to treat and prevent allergies, infectious diseases, and chronic inflammatory diseases using versatile, proprietary approaches that alter immune system responses in highly specific ways. Our clinical development programs are based on immunostimulatory sequences, or ISS, which are short DNA sequences that enhance the ability of the immune system to fight disease and control chronic inflammation. ISS are being developed in three initial indications: ragweed allergy immunotherapeutic, currently in a Phase 2/3 clinical trial; a Hepatitis B vaccine that has completed a Phase 2 clinical trial; and an asthma immunotherapeutic that has completed a Phase 2 exploratory trial.

Under the terms of an agreement established in 2004 with UCB Farchim, S.A., a subsidiary of UCB, S.A., a publicly traded multi-national company based in Brussels, Belgium, UCB has an option to license Dynavax' peanut allergy program.

Dynavax cautions you that statements included in this press release that are not a description of historical facts are forward-looking statements, including without limitation all statements related to plans to advance its peanut allergy program toward clinical trials, to advance its clinical programs in ragweed allergy, hepatitis B and asthma, and to demonstrate the potential of its ISS technology. Words such as "believes," "anticipates," "plans," "expects," "intend," "will," "slated," "goal" and similar expressions are intended to identify forward-looking statements. The inclusion of forward- looking statements should not be regarded as a representation by Dynavax that any of its plans will be achieved. Actual results may differ materially from those set forth in this release due to the risks and uncertainties inherent in Dynavax's business including, without limitation, risks relating to: the progress and timing of advancing its peanut allergy program into clinical testing; the progress and timing of its clinical trials in ragweed allergy, hepatitis B and asthma; difficulties or delays in developing, testing, obtaining regulatory approval of, producing and marketing its products; the scope and validity of patent protection for its products; competition from other pharmaceutical or biotechnology companies; its ability to obtain additional financing to support its operations; its ability to maintain effective financial planning and internal controls; and other risks detailed in the "Risk Factors" section of Dynavax's Annual Report on Form 10-K filed on June 30, 2004, and in the section titled "Additional Factors That May Affect Future Results" within Dynavax's quarterly report on Form 10-Q filed on November 8, 2004. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and Dynavax undertakes no obligation to revise or update this news release to reflect events or circumstances after the date hereof.

SOURCE Dynavax Technologies Corporation

Jane M. Green, Ph.D., Vice President, Corporate Communications of Dynavax Technologies Corporation, 510-665-4630, or jgreen@dvax.com

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