REPRINT FROM MARCH 26, 2012

BioCentury

THE BERNSTEIN REPORT ON BIOBUSINESS™



*Emerging Company Profile*

# ImmusanT: Having their cake

**By Erin McCallister**
**Senior Writer**

**ImmusanT Inc.** is developing what could be the first treatment for celiac disease that allows patients to eat a normal diet. The company's Nexvax2 vaccine seeks to reprogram CD4+ T cells to induce gluten tolerance.

The biotech also is developing a blood-based companion diagnostic. Both programs were acquired from **Nexpep Pty. Ltd.**, which is now a shell company.

Celiac disease is an immune-mediated disorder triggered by consumption of foods containing gluten, which is broken into immunogenic peptides that are allowed to pass through the intestinal epithelium.

The peptides are taken up by antigen-presenting cells (APCs) and presented to CD4+ T cells, which in turn secrete proinflammatory cytokines and trigger a B cell response to produce antibodies against the peptides.

Other than a gluten-free diet, no treatment exists for the disease, which is characterized by severe intestinal damage, nutrient malabsorption, diarrhea, fatigue and weight loss. It is very difficult to eliminate all gluten consumption, and accidental ingestion of even trace amounts can result in acute attacks.

Nexvax2 is an intradermal vaccine that combines a 15-16 amino acid fragment from each of three immunogenic peptides that are products of the breakdown of gluten by enzymes in the lumen of the small intestine: wheat alpha gliadin, wheat gamma gliadin and barley hordein.

## ImmusanT Inc.

Cambridge, Mass.

Technology: Therapeutic celiac disease vaccine

Disease focus: Autoimmune

Clinical status: Phase I

Founded: 2010 by Leslie Williams

University collaborators: Walter Eliza Hall Institute of Medical Research, Monash University, University of Melbourne

Corporate partners: None

Number of employees: 4

Funds raised: $21 million

Investors: Vatera Healthcare Partners

CEO: Leslie Williams

Patents: 4 issued covering diagnostic and therapeutic use of peptides of wheat alpha gliadin, wheat gamma gliadin and barley hordein

Robert Anderson, CSO of ImmusanT and former professor at the **Walter and Eliza Hall Institute of Medical Research**, discovered that these three protein fragments are responsible for a T cell response in the 80-90% of celiac disease patients who carry the major histocompatibility complex class II DQ2 (HLA-DQ2) gene.

ImmusanT expects administering very small fragments of the proteins will "shift the patient's T cell phenotype from a proinflammatory to a tolerant phenotype," President and CEO Leslie Williams said.

The mechanism is not fully understood, but Nexvax2 activated gluten-specific T cells in transgenic mice, and with repeated dosing eliminated proinflammatory cytokine secretion by the T cells. The T cells also were unable to proliferate and regulatory T cells became enriched.

Last May, data from a double-blind Phase I trial in 34 celiac patients showed weekly doses of up to 90 µg of Nexvax2 for three weeks were well tolerated.

Next quarter, ImmusanT plans to start two trials to assess the safety and tolerability of the vaccine in HLA-DQ2-positive celiac patients: a Phase Ib trial in Australia and a Phase I U.S. trial.

ImmusanT is developing a panel of immunologic diagnostics to monitor T cell response during trials. The company also will assess how long memory T cells persist in celiac patients to determine how

*See next page*

BioCentury®
THE BERNSTEIN REPORT ON BIOBUSINESS

PO Box 1246
San Carlos CA 94070-1246
Voice: 650-595-5333
Fax: 650-595-5589
www.biocentury.com

DAVID FLORES
President & CEO

KAREN BERNSTEIN, Ph.D.
Chairman & Editor-in-Chief

***Emerging Company Profile,***
*from previous page*

long patients should be gluten-free before starting treatment.

Patients in upcoming trials will begin with a 30-day gluten free diet, followed by a gluten challenge, which is standard practice in diagnosing celiac disease. Patients would then be assessed for T cell response using ImmusanT's diagnostic, which is in early validation testing.

"Patients who are HLA-DQ2-positive may not always have a T cell response," Williams said. "Thus, our test identifies those HLA-DQ2 patients who will respond to the vaccine."

Patients who test positive would again be put on a strict gluten-free diet for 30 days, after which treatment would begin.

ImmusanT will evaluate different dosing regimens in the trials, but envisions an induction/maintenance regimen similar to that used in allergy immunotherapy injections, starting with low doses administered over a yet-to-be determined period of time in a physician's office.

In the maintenance phase, patients would self-administer weekly or bi-monthly injections while returning to a normal diet. Despite the risk of an acute reaction, Williams believes most patients want to return to a normal diet and will do so in the clinical trial.

In contrast to allergy immunotherapy, Williams said, self-injection should be possible because the 15-16 amino acid peptide fragments are not long enough to crosslink with IgE on the surface of mast cells, overcoming the potential of anaphylaxis.

ImmusanT expects to partner the vaccine for development and commercialization.

Two other companies have disclosed clinical programs for celiac disease, but both are being developed as an adjunct to a gluten-free diet. **Alvine Pharmaceuticals Inc.**'s ALV003 is an oral, once-daily combination of cysteine protease (EP-B2) and a proline-specific propyl endopeptidase (PEP) engineered to degrade gluten. It is in Phase II testing.

Larazotide (AT-1001), a zonulin receptor antagonist from **Alba Therapeutics Corp.**, also is in Phase II testing. Cephalon Inc., a unit of **Teva Pharmaceutical Industries Ltd.**, has an option to the oral synthetic peptide that targets the tight junction protein to block intestinal permeability to gluten.

COMPANIES AND INSTITUTIONS MENTIONED

**Alba Therapeutics Corp.**, Baltimore, Md.
**Alvine Pharmaceuticals Inc.**, San Carlos, Calif.
**ImmusanT Inc.**, Cambridge, Mass.
**Nexpep Pty. Ltd.**, Ivanhoe, Australia
**Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA), Petah Tikva, Israel
**Walter and Eliza Hall Institute of Medical Research**, Melbourne, Australia