

ImmusanT Seeks to Restore Gluten Tolerance with Vaccine

By Marie Powers

BioWorld Today Contributing Writer

Privately held ImmusanT Inc. has become the newest entrant in the wide-open race to find a drug therapy for the inherited autoimmune disorder celiac disease. The company established operations this month in Cambridge, Mass., with the goal of developing an immunotherapeutic vaccine, companion diagnostic and monitoring tool for celiac disease, which is triggered by foods containing gluten – the main protein in wheat, rye and barley.

When individuals with celiac disease consume gluten, their immune systems respond by triggering T cells to fight the offending proteins, damaging the small intestine and inhibiting the absorption of nutrients into the body. Because no drug therapy is available, the only treatment for individuals with the disease – approximately 1 percent of the global population – is to eliminate gluten from the diet. However, compliance is challenging, and untreated disease in adults is associated with increased risk of fractures and osteoporosis, problems during pregnancy and birth, short stature, dental enamel hypoplasia, dermatitis, recurrent stomatitis and cancer.

About a year ago, Bob Anderson, a professor at the Australian Walter and Eliza Hall Institute and CEO of the Australian biotech start-up Nexpep Pty Ltd., was in Boston giving a lecture series as part of a sister city collaboration between Boston and Melbourne. Anderson, a gastroenterologist, had discovered the three primary peptides responsible for making gluten toxic to people with celiac disease, and Nexpep was in the midst of a Phase I trial of a vaccine designed to desensitize individuals with gluten allergy.

A decade earlier, Anderson had proven that celiac disease could be studied in blood samples of individuals with the disease, not just biopsies of gut tissue, supporting the view that celiac precipitated a whole-body immune response. Subsequently, Anderson and colleagues studied the amino acid sequences that prompt T cells to trigger the allergic response to gluten characteristic of celiac disease. Instead of alpha-gliadin – long considered the main culprit – the researchers discovered that problematic amino acid sequences result from a trio of sequences that come from

omega-gliadin in wheat, and two other proteins, hordein and secalin, that have equivalent roles to gliadins in rye and barley. The scientists published their findings last year in *Science Translational Medicine*. (See *BioWorld Today*, July 28, 2010.)

Nexpep had raised about A\$6 million (US\$5.4 million) but didn't have the resources to take its vaccine technology to the next level, so Anderson had been talking with seasoned entrepreneurs and venture capitalists about options to move the celiac disease platform forward.

Enter Leslie Williams, who had pharmaceutical industry experience at Merck & Co. Inc., GlaxoSmithKline plc and INO Therapeutics and was a venture partner at Battelle Ventures. Williams also had served as president and CEO of Ventaira Pharmaceuticals, of Columbus, Ohio. Anderson and Williams connected through Boston's ecosystem, and a one-hour lunch lasted until late in the afternoon while the two discussed Nexpep's technology, platform and market opportunity.

After conducting due diligence on the company, Williams met with Anderson and Nexpep's board in Australia to advise them about options for a corporate restructuring, including the prospect of moving to the U.S., where Nexpep would have more attractive funding prospects. She declined an offer to serve as the company's CEO in Australia.

Instead, with the board's blessing, Williams developed a business plan and secured seed financing from angel investors. In December 2010 she formed ImmusanT to acquire the IP from Nexpep, which fulfilled its corporate obligations in Australia and subsequently ceased operations. Williams was named president and CEO of ImmusanT while Anderson joined the company as chief scientific and medical officer. The two, along with a part-time chief financial officer, are the company's only employees.

ImmusanT's product pipeline includes Nexvax2, a therapeutic vaccine that combines the three proprietary peptides that elicit an immune response in patients with celiac disease who carry the immune recognition gene

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HLA-DQ2. Nexvax2 is delivered intradermally in small doses to reprogram and desensitize the disease-causing T cells triggered by a patient's immune response to gluten. The approach is similar to treatments for allergies to cats, ragweed or dust mites, where repeated doses establish tolerance to a specific antigen. In the case of celiac disease, the repeated doses reduce or eliminate the body's rejection of dietary gluten.

By reprogramming the T-cell response, the Nexvax2 approach is designed to reduce inflammation in the villi that line the small intestine and are responsible for absorbing nutrients, thus returning the intestine to a normal healthy state.

A Phase I safety, tolerability and bioactivity study of Nexvax2 was completed last year, and the company plans to present data from the study at Digestive Disease Week in Chicago in early May. A Phase IIa trial of the vaccine is expected to begin in the next 12 months, according to Williams.

In addition to the vaccine technology, ImmusanT has a commercial agreement with INOVA Diagnostics Inc., of San Diego, to develop improved serology diagnostic screening tests for celiac disease that might eliminate the need for surgical biopsies of the small intestine. ImmusanT's simple whole-blood ELISA companion test would measure the activity of T cells causing celiac disease and also could be used to monitor optimal maintenance of immune tolerance with Nexvax2.

Nexpep had planned to divest the diagnostic application – a move Williams strongly opposed. Pairing the companion diagnostic with the therapeutic vaccine “is a powerful combination” that broadens the company's potential commercial market, she explained. Moreover, “from a regulatory standpoint, we can much better identify our subpopulation where this therapeutic will be effective,” she told *BioWorld Today*. “I wanted to continue to control that part of the business.”

The company's diagnostic for celiac – which could be marketed as a companion or standalone tool – as well as its

approach to focus on the HLA-DQ2 subtype and to treat the underlying disease “as an autoimmune disease with an allergic component” are the fundamental differentiating strategies for ImmusanT, a name that roughly translates from Latin as “free of health constraints” using “T” cell therapeutics.

“We're focused on tricking the immune system into reprogramming the T cells so they're not recognized as foreign components,” Williams said. “We intend to allow patients to return to a normal diet.”

The name is equally applicable to additional applications for the company's immunotherapy discovery platform, which may include a variety of epitope-specific autoimmune diseases, such as Type I diabetes and irritable bowel syndrome, she added.

Although Williams declined to specify the amount of funding raised from angel investors, the company's plan is to “prepare to get in front of the FDA as soon as possible.” By outsourcing much of its development work to contract research organizations, ImmusanT has a sufficient financial runway for that effort, and the company has the option of bringing in additional seed capital, if needed, Williams said.

Long term, the company will seek to link with a large pharma, either through a strategic collaboration or outright acquisition.

If its technology succeeds, the company might have its pick of partners, as competition in the celiac disease space is sparse. Last month, Cephalon Inc., of Frazer, Pa., paid \$7 million to pick up an option for midstage celiac disease candidate larazotide acetate from struggling private biotech Alba Therapeutics Inc., of Baltimore. (See *BioWorld Today*, Feb. 11, 2011.)

A more formidable rival may be privately held Alvine Pharmaceuticals Inc., of San Carlos, Calif., which has attracted a bevy of investors in its efforts to develop ALV003, an oral mixture of a glutamine-specific cysteine protease and a proline-specific prolyl endopeptidase, in celiac disease. ■