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Get a Shot, Have Some Bread: ImmusanT's Plan For a Celiac Vaccine

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For people with celiac disease, there's one way to avoid symptoms: don't eat gluten. But what if a vaccine and some booster shots could let you eat all the wheat-filled food you want, without all the nasty consequences? That's the kind of thing a Cambridge, MA-based startup called ImmusanT is trying to prove is possible.

Sometime within the next few months, ImmusanT will likely report data from two separate early-stage clinical trials for a vaccine, NexVax2, that it's developing for celiac disease—an autoimmune disorder in which eating gluten triggers a sufferer's immune system to attack his small intestine. Those data, from two separate studies in the U.S. and Australia, will represent the first signals as to whether ImmusanT is on to something in treating celiac disease. It's also the first move in a broader effort to prove that the company's concept of a peptide immunotherapy platform is viable.

"It's a very exciting first half of the year with the data that is pending," says CEO Leslie Williams.

Of course, even if those studies are a success, they're really the first step down a long road for ImmusanT. These two studies are Phase 1b trials, designed to make sure NexVax2 is safe and to find a range of potential doses the company might be able to use in its next studies. There will be several clinical hurdles to come. Meanwhile, there are plenty of other companies trying to find treatments for celiac disease. Both San Carlos, CA-based Alvine Pharmaceuticals and Baltimore, MD-based Alba Therapeutics, for instance, are developing drugs that are supposed to be taken in combination with a gluten-free diet. Sitari Pharmaceuticals, a startup emerging from a joint venture between GlaxoSmithKline and Avalon Ventures, recently raised $10 million to pursue treatments for the digestive disorder.

But even with all those forces raging around ImmusanT, Williams says that the company stands out for one key reason: if its plan succeeds, celiac patients might one day be able to eat all the gluten they want.

"We are the only treatment in development to date that is disease-modifying," she says. "Our focus is disease modification so patients can resume an unrestricted diet."

ImmusanT
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When people with celiac disease digest gluten—a protein found in wheat, barley, and rye—their immune system mistakes certain fragments of the protein as invaders and mounts an attack. This causes inflammation and damage in the intestine, impairing its ability to absorb nutrients and leading to things like abdominal pain, vomiting, and diarrhea. Left untreated, celiac can lead to much more significant problems, such as growth delays, osteoporosis, or infertility. Celiac disease affects about 3 million people in the U.S., though only about 10 percent of them are officially diagnosed through an intestinal biopsy, Williams says.

Right now, the only real option for celiac patients is to completely avoid gluten. ImmusanT's idea, however, is to inject patients with a vaccine containing engineered version of the three gluten fragments that trigger the immune response in most celiac patients. These peptides, each about 15 amino acids long, are supposed to train the immune system to see gluten as food, so it doesn't trigger an attack in the gut.

The approach may sound a little counter-intuitive, given that most vaccines teach the immune system to attack the injected molecules. But Williams likens the company's approach to allergy shots, which help the body gradually learn to tolerate a particular allergen through a regimen of periodic injections. In ImmusanT's case, injecting small amounts of the problematic peptides, at regular intervals, is supposed to "reprogram" patients' immune systems, she says.

"[This] switches off disease-causing T-cells and induces clinical tolerance," Williams says of the therapy. "It resets the way the body responds immunologically."

The regimen ImmusanT is anticipating would be a two-step program. First, patients go through an "induction phase" managed by a physician. The length of this phase hasn't been worked out in clinical trials as of yet, but ImmusanT envisions that patients would get one to two shots per week for approximately eight weeks to induce tolerance to gluten.

Patients, in theory, would then be able to eat gluten after that point, though ImmusanT believes they would need periodic booster shots at a frequency that the company hasn't yet determined, according to Williams. The company has also developed a blood test that will help ImmusanT select responders to its treatment, and periodically monitor the status of their response, she says.

ImmusanT was formed around discoveries that immunologist Bob Anderson made more than a decade ago at the University of Oxford. Anderson, ImmusanT's scientific founder and chief scientific officer, discovered peptides that appear to trigger the immune response in patients with the most common genetic subtype of celiac disease—those with copies of the gene HLA-DQ2.5. He then made small, synthetic versions of them, and formed Melbourne, Australia-based Nexpep around his work in 2005.

Anderson, however, wanted to develop the technology in the U.S. and met with Williams, then a venture partner at VC firm Battelle Ventures, for help. At the time, Williams was looking to spin technologies out of MIT, but she became intrigued by Anderson's work.

"I immediately saw how this could be leveraged more broadly beyond celiac disease," she says, noting that various subsets of celiac patients also end up with other autoimmune disorders like type-1 diabetes and rheumatoid arthritis.

ImmusanT CEO
Leslie Williams

So Williams and Anderson hammered out a licensing deal for the assets of Nexpep, and turned them into ImmusanT in December 2010. Williams was then able to secure $1 million in seed funding from sources she declined to name to get the company to the cusp of its first clinical trial, and then, in late 2011, landed a $20 million Series A equity financing from New York-based Vatera Healthcare Partners to begin bankrolling the first studies.

Williams then rounded out the executive team. Anderson moved from Australia to Boston and came aboard as chief scientific officer, and former Shire executive Ferdinand Massari joined up as chief medical officer. ImmusanT opened up its own immunology lab in Kendall Square. Though it currently has just six full-time employees, the company plans to hire more staff to fill research roles, and potentially some marketing positions, when it moves towards its next trial, according to Williams.

"We need to emphasize diagnosis and awareness," she says of why the company might hire marketing reps at such an early stage.

First, however, ImmusanT has to accrue data. The company is attempting to manage its development risk by tailoring its immunotherapy—and its clinical trials—to patients carrying the HLA-DQ2.5 gene, believing they'll best respond to the vaccine.

If the two ongoing Phase 1b trials are successful, the type of studies ImmusanT would have to run next are unclear. Williams says that ImmusanT would have to look at the data it generated and meet with the FDA to define goals in future studies with the agency. But the big plan is to ultimately use celiac disease as a test case for its peptide immunotherapy as a platform.

"Celiac disease is an ideal model for autoimmune disease because we know the genes, we've defined the antigens that trigger the immune response, we can monitor that with a diagnostic tool, and you can access the organ, the small intestine, with an endoscopy," she says. "The premise is to take what our learnings are [here] and look at a variety of genetically similar diseases."

Should ImmusanT prove it's at least on to something, the company, which Williams says currently has enough funds to last through the end of 2014, might have some financing choices other than just another private round.

"We're entertaining many options right now," Williams says.

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