2022 SUMMER **RESEARCH REPORT**

July 25, 2022

Accelerating research for treatments and a cure for celiac disease is the top priority of the Celiac Disease Foundation. Supporting cost-efficient patient recruitment to critical clinical trials for potential celiac disease therapies is one of the many ways we accelerate research. The only path to an FDA-approved treatment is through a carefully structured, scientifically rigorous, and incredibly expensive 3-phase clinical trial process. Through use of our research tools, iCureCeliac® and iQualifyCeliac, and with the approval of our Medical Advisory Board, we help to lower the cost of finding patients to participate in clinical trials, keeping more potential therapies moving through the drug development pipeline than would otherwise be possible.

As you likely know by now, 9 Meters, one of our biopharmaceutical partners, announced that they are discontinuing their Phase 3 trial for their treatment, larazotide, referred to as CedLara. An independent analysis at an interim phase in the trial concluded that a substantial number of new patients would have to be enrolled in the trial to demonstrate statistical significance of the drug's efficacy. 9 Meters concluded that the number of patients required to compare a placebo to larazotide was too large to support their trial continuation.

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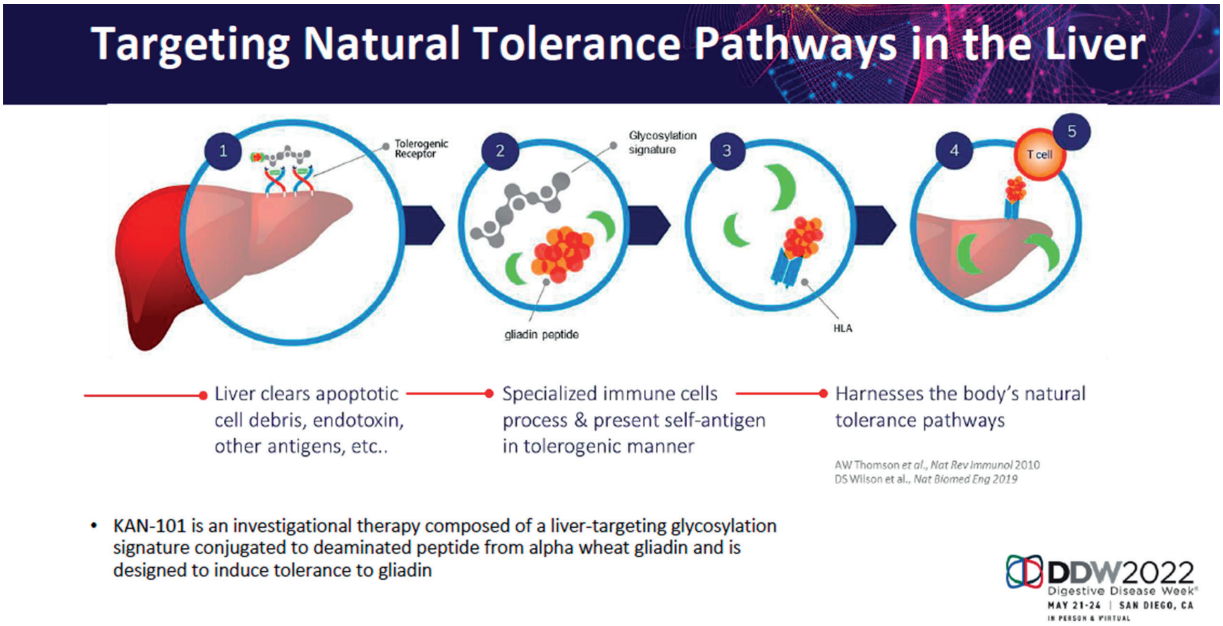
Larazotide was the only celiac disease drug in Phase 3 clinical trials. While we are disappointed by the cancellation of the trial, we understand the enormous risk involved in drug development. We also appreciate that 9 Meters will continue to analyze the trial data to determine further plans for larazotide, and that the discoveries made in the larazotide development process will be invaluable to researchers trying to unravel celiac disease treatments and, one day, a cure.

We are optimistic that the current surge of research will produce the first FDA-approved treatment for celiac disease. Our optimism comes from the variety of approaches biopharmaceutical companies are taking to treat the disease to make it easier for patients to manage and thrive. We have prepared this Summer Research Report to highlight the variety of biochemical approaches potential celiac disease drugs are taking. The Celiac Disease Foundation is proud to be a partner with each of the companies researching these drugs, using our tools to accelerate the research process.

Anokion: KAN-101

One of the Phase 1 clinical trials we supported in 2021 was for a novel treatment, KAN-101, developed by the biopharmaceutical company, Anokion. At Digestive Disease Week (DDW) this past May, the Anokion research team, led by Celiac Disease Foundation Medical Advisory Board Member and recipient of the first inaugural Celiac Disease Foundation Prize for Excellence in Celiac Disease Research, Dr. Joseph Murray of Mayo Clinic, announced the findings of the Phase 1 trial. We would like to share with you some of those findings, as the **approach Anokion is taking to treat celiac disease is unique and, if successful, not only holds promise for celiac disease, but also for many other diseases.**

Anokion's approach is to engineer immune tolerance. Patients suffering from autoimmune diseases harbor immune cells that mistakenly recognize and attack the body's own cells as foreign entities. When people with celiac disease ingest gluten, these immune cells produce inflammation, damaging the body's organs and tissues and causing symptoms and long-term health complications. KAN-101 works by delivering a gluten antigen to the liver to educate the immune system to ignore gliadin, the component of gluten that many researchers believe triggers the gluten response in celiac disease patients. The goal of this education process is to create immune tolerance while also leaving the rest of the immune system untouched.



The KAN-101 team announced at DDW that the Phase 1 trial of the drug was a success. There was no discernable increase in liver function in the study group, a sign that the KAN-101 caused no harm to the liver. Adverse effects of the drug were "mild to moderate" gastrointestinal symptoms typically seen in celiac disease (the drug contains gliadin, so the reaction was expected) and were resolved in a few hours and with treatment for the symptoms. On the heels of the promising results for KAN-101 in its Phase 1 trial, **Anokion has received permission from the FDA to begin a Phase 2 trial to more specifically test efficacy and dosage.**

ImmunogenX: Latiglutenase

Latiglutenase from the biopharmaceutical company ImmunogenX is a dual enzyme drug designed to break down gluten in the stomach into small, harmless fragments, reducing the gliadin immune response in people with celiac disease. It is a drink-based medication intended to be taken at meals to help relieve common symptoms suffered by celiac disease patients after accidental gluten exposure. **In Phase 2 trials supported by the Celiac Disease Foundation, self-reported relief for abdominal pain, bloating, tiredness, and constipation was pronounced in celiac disease patients who continued to test positive for gluten-induced antibodies in their blood (seropositive).**

Latiglutenase was originally developed by Alvine Therapeutics with the goal of advancing healing in the gut of celiac disease patients. While this goal was not achieved, the Celiac Disease Foundation is providing patient recruitment for ImmunogenX as it investigates latiglutenase for improvement in symptomatic patients in its Solutions for Celiac Phase 2 trial.

Provention Bio: PRV-015

The novel drug PRV-015, also known as AMG 714, targets yet another pathway to mitigate the impact of gluten in people with celiac disease. PRV-015 is an antibody designed to block an immune system protein called interleukin-15, also known as IL-15. Gluten ingestion in people with celiac disease results in the production of IL-15, which triggers intestinal inflammation that leads to the destruction of intestinal cells. Originally developed by Amgen for rheumatoid arthritis, it is now being co-developed for the treatment of gluten-free diet non-responsive celiac disease (NRCD) by Provention Bio with the aims of reducing both symptoms and intestinal inflammation and damage caused by accidental gluten exposure.

Already tested in approximately 250 people in six completed research studies, **PRV-015 has shown to be well-tolerated, and it may reduce inflammation and improve the symptoms of celiac disease.** The Celiac Disease Foundation is currently recruiting for the Proactive Celiac Study Phase 2b trial in the United States and Canada.

Takeda: TAK-101, TAK-062, and the Virtual Celiac Symptoms Study

Takeda Pharmaceuticals has emerged as one of the major players in the celiac disease drug space. They have procured rights for two potential therapies from smaller biopharmaceutical companies, with both heading into Phase 2 clinical trials this fall.

TAK-101

Takeda licensed TAK-101 (formerly CNP-101 or TIMP-GLIA) from Cour Pharmaceuticals in 2019. TAK-101 is an immune modifying nanoparticle containing gliadin proteins. It is designed to bind with immune cells called monocytes and load them with gliadin proteins. The cells travel to the spleen where the gliadin is released, reprogramming the immune system to tolerate gluten as a non-threatening substance and negating or reversing the signs and symptoms of celiac disease without using immune suppressing drugs.

TAK-062

TAK-062 (formerly Kuma062) is a highly potent super glutenase – a protein that degrades ingested gluten – developed by PvP Biologics that Takeda acquired after a successful Phase 1 proof-of-mechanism study. TAK-062 is designed to degrade the immune-reactive parts of gluten before they exit the stomach in order to prevent an immune response. Unlike other glutenase drugs that have been tested for celiac disease, TAK-062 is specifically engineered to better target gluten and to survive the acidity of the stomach. **TAK-062 has shown robust gluten degradation in humans and holds great promise to alleviate suffering among celiac patients.**

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Virtual Celiac Symptoms Study

To better understand the symptom patterns and impacts of celiac disease to inform drug development, Takeda, together with the Celiac Disease Foundation, is launching a study where participants will download an app to their smartphone and answer daily questionnaires about their symptoms and life with celiac disease for 12 weeks. Patients ages 12 and up with a confirmed diagnosis of celiac disease will be eligible to participate in this study, launching late summer.

Conclusion

The Celiac Disease Foundation is, or will soon be, supporting seven clinical trials, two Phase 1 and five Phase 2. Recruiting celiac disease patients is challenging and expensive, often prohibitively so. A few reasons for the difficulty include:

- It is estimated that only about 30% of the celiac disease population has been properly diagnosed.
- Long-term health implications of celiac disease are poorly understood.
- Researchers need biopsy-confirmed celiac patients for clinical trials, which has become increasingly more difficult to find as many diagnoses of celiac disease are made by primary care physicians based upon tissue transglutaminase IgA antibody (tTG-IgA) results without a referral for biopsy.
- Patients who agree to participate in clinical trials are often subjected to gluten challenges as a precursor to testing the effectiveness of a proposed therapy.

There will be no approved treatments or a cure for celiac disease without clinical trials. That means there will be no approved treatments or a cure for celiac disease if we can't find patients willing to participate in clinical trials.

iCureCeliac®, the Celiac Disease Foundation Patient Registry, is the best tool we have to identify and recruit patients for all types of celiac disease research, including for clinical trials. iQualifyCeliac, our Study Screening Platform built specifically to identify clinical trial and research study prospects, is our other powerful tool. Currently, we have about 9,600 patients in iCureCeliac®. We need to grow these databases dramatically to more effectively support critical research in celiac disease.

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This is our plan of action:

- We have launched a national campaign to recruit patients to participate in iCureCeliac®.
- We have commissioned and released a new short film, "Curing Celiac: A Short Story," from filmmaker, Hayley Repton, to highlight the benefits of iCureCeliac® to the celiac patient community.
- We have partnered with Schär to provide a thank you gift of gluten-free products to new iCureCeliac® participants.
- We ask you to share with us your ideas of how to encourage patients to enroll in clinical trials.

The variety and quality of approaches to treating celiac disease from our biopharmaceutical companies is incredibly encouraging. This is the kind of work your generous donations to the Celiac Disease Foundation support. If you are able, please make a tax-deductible gift today. Your continuing support sustains us.

If you have ideas on how to best recruit celiac patients to participate in trials and studies, or any questions about this Summer Research Report or iCureCeliac®, please don't hesitate to reach out.

Warmest regards,

Marilyn G. Geller
Chief Executive

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