Beyond Celiac 2019 Research Summit, *Getting Over the Peak:*

The Final Ascent to Realizing Therapies in Celiac Disease

Executive Summary

The November 15, 2019 Beyond Celiac Research Summit, *Getting Over the Peak: The Final Ascent to Realizing Therapies in Celiac Disease*, brought together a group of 50 stakeholders representing clinician scientists, patients, drug developers, patient advocacy group leaders, a private health insurer and the United States Food and Drug Administration (FDA). The summit provided a unique opportunity for all celiac disease stakeholders to elucidate the challenges to developing non-dietary therapies for celiac disease.

Through eight informative panels, the summit identified challenges with conducting clinical trials in celiac disease and generated 15 broad ideas for accelerating drug development of new therapies intended to treat celiac disease.

Patient panels affirmed the seriousness of the psychosocial burden of the gluten-free diet, pinpointing inadequate education of patients/providers as barriers to progress. Barriers to clinical trials identified by all panels include participant identification, optimization of trial design, insufficient communication with participants, need for refinement of the gluten challenge, and the effect of participant behavior on trial outcomes.

Health insurance coverage for new drugs to treat celiac disease could be hindered by insurance company's lack of awareness of the challenges of the gluten-free diet and the patient burden of disease. From the payer perspective other barriers include lack of data on the medical costs of celiac disease and evidence of the value of therapies and identification of the groups of patients who would benefit from new therapies.

Solutions that emerged included: educating patients/caregivers to advocate for therapy development; developing a celiac disease patient passport to include all relevant medical information; creating best practices for clinical trials; encouraging collaboration of advocacy groups to activate grass roots calls for therapies; considering the incorporation of adolescents into clinical trials in adult patients with celiac disease; and quantifying real costs of celiac disease to payers and society.

Stakeholders unanimously called for a series of follow-up sessions to continue to fine tune the discussion of barriers, their solutions and the role of each stakeholder group. Beyond Celiac will lead this ongoing collaboration.

Beyond Celiac Objectives

The unmet medical need in celiac disease is significant. The only current treatment is disease management through the gluten-free diet, which is not fully effective for many patients and is associated with high treatment burden and significant psychosocial impact on patients and families.

The mission of Beyond Celiac is to advance new treatments for celiac disease and, eventually, find a cure. Additionally, the organization is committed to bringing the patient voice to the process, as patient participation in clinical trials has repeatedly been identified as a critical element, including in Beyond Celiac Research Symposiums in 2017, 2018 and 2019.

As a trusted resource among celiac disease patients and caregivers, Beyond Celiac identified a need to bring all stakeholders together to detail and discuss the primary barriers to getting new treatments to patients. While increased activity in the study of new treatments for celiac disease is encouraging, the long path to approval is recognized, reflecting the challenges of making new medicines available to patients.

While multiple celiac disease clinical trials have been performed and 49 studies investigating new treatments are underway, there is need for refining study design and endpoints. There are currently no drugs approved by the FDA for the treatment of celiac disease. Strategies to ensure reimbursement from payers and to increase funding for research remain largely undeveloped.

Consequently, the primary goals of the summit were to:

- Identify remaining barriers to developing new therapies for adults and children with celiac disease
- Outline tangible, feasible, immediate mid- and long-term action items and strategies for individual stakeholder groups and the celiac disease community as a whole.

Format and Methods

The Beyond Celiac Research Summit was held November 14-15, 2019 in Baltimore, MD. The first evening of the summit, Bob Beall, PhD, a member of the Beyond Celiac Board of Directors and Scientific Advisory Council and former president and CEO of the Cystic Fibrosis Foundation, gave the keynote address providing the framework for the role advocacy groups can have in successfully accelerating therapies.

In the all-day meeting Friday, fifty stakeholders in six unique groups (see Appendix 1 for full list) participated, including:

- Adult and pediatric clinician scientists
- Patients
- Drug developers
- Patient advocacy leaders
- Private health care insurance

- Food and Drug Administration representatives

The stakeholders formed eight informative panels:

1. Patient Panel I- The burden of celiac disease and the gluten-free diet
2. Patient Panel II- Firsthand experience participating in a clinical trial
3. Update on current therapies in the pipeline
4. The drug developer perspective
5. The FDA perspective
6. The payer perspective
7. How and whether to include children in clinical trials
8. The role of patient advocacy groups in getting therapies to patients

In advance of the summit, members of each panel identified barriers to therapeutic development in their own stakeholder group, in other groups and in society (See Table 1). During the workshop, topics were presented by individual stakeholder panels followed by full group discussion to allow cross-fertilization within and across stakeholder groups. From the identified barriers, solutions and next steps were delineated within and across stakeholder groups.

Audio of the full summit was recorded and a written transcript of the proceedings was compiled. This document was written by Beyond Celiac staff based on the transcript and reviewed by participating stakeholders. The two patient panels and the update on current therapies were available live via webcast and are currently available on the Beyond Celiac website.[1]

Patient Panel I – The burden of celiac disease and the gluten-free diet.

A panel of patients who addressed the overall difficulty of living with celiac disease noted that, unlike other conditions, the burden is not adequately recognized by the outside world. The burden is substantial, and often includes a significant negative impact on quality of life by limiting social activities and educational and employment opportunities.

At home, celiac disease patients and caregivers have control over the gluten content and safe preparation of the food they eat, but when they eat out there is always a risk of gluten exposure. The constant focus of finding safe food on the gluten-free diet reduces time and energy for other aspects of life. Traveling for fun or work carries the extra stress of needing to find safe food. Additionally, the whole family, not just the person who has celiac disease, is affected. Diagnosis is often delayed and celiac disease awareness and expertise is still limited among healthcare providers.

While many patients are burdened by symptoms of celiac disease, both intestinal and extra-intestinal, a panelist who is asymptomatic said it is challenging to accept that a gluten-free diet is necessary. Asymptomatic patients also do not feel better when they initiate a gluten-free diet,

[1] https://www.youtube.com/watch?v=AAM8YBFCBjo

removing one of the motivators for being adherent and providing evidence that new treatments are needed for both those with symptoms and without symptoms.

Patient Panel II – Firsthand experience participating in a clinical trial

Patients who had participated in at least one completed clinical trial described experiences that ranged from very positive to disappointing and alienating. Study participants identified communication from researchers after a trial had ended as a key factor in determining how they felt about their experience. Study participants wanted more information about the study group they had been in, i.e. treatment or placebo, any health records generated and kept, including serology and histology, and the overall results of the study. Lack of post-trial communication and information was described as the most negative part of being a study participant.

One study participant whose symptoms were relieved by the treatment she suspected she had received during a trial described a sense of loss when the treatment was no longer available after the trial.

Helping others with celiac disease by being part of the advancement of new therapies was cited as the main reason panelists participated in studies. Other benefits included compensation, updated biopsies and blood tests, which sometimes led to detection of other conditions, and other diagnostic tests that could detect otherwise unknown health problems.

In addition to more information about the trial and its results, patients agreed that being able to get some study assessments done closer to home would be helpful, particularly because travel sometimes necessitates taking a day off from work. Panelists agreed that when a gluten challenge is part of a study, researchers should try to offer something that is more palatable than what is typically used in clinical trials.

Update on current therapies

Joseph Murray, MD, a celiac disease expert at the Mayo Clinic and a member of the Beyond Celiac Scientific Advisory Council, updated summit attendees on the current state of drug development. Drugs under study have been designed with the potential to treat celiac disease in two broad strategies: interrupting the inflammatory response to gluten in an unchanged immune system and inducing tolerance to gluten by reprograming the immune system.

While some clinical trials have had encouraging results, others have had disappointing outcomes, in particular the Nexvax2 trial, which was discontinued prematurely when the primary endpoint (symptomatic improvement) was not reached. One therapy under development is currently being evaluated in phase 3 of development. There are a number of other potential treatments in earlier phases of drug development.

Clinical trials are feasible both with and without a gluten challenge. However, when a trial is designed to prevent the effects of gluten it can't demonstrate success unless it can be assured that study participants are consuming gluten.

Drug developer perspective

The panel of pharmaceutical company representatives reviewed reasons therapeutics are needed in celiac disease, namely: there are no approved non-dietary treatments for celiac disease; despite best efforts at the gluten-free diet, as little as 50 mg/day of gluten can trigger inflammation,[2] gluten exposure leads to continued symptoms in patients with celiac disease,[3] patients are dissatisfied with the gluten-free diet,[4] and the high cost of gluten-free foods adds to burden of the gluten-free diet.[5]

Panelists identified a lack of early-phase translatable markers of celiac disease as a challenge. These non-invasive markers, if identified, may allow for earlier identification of efficacy and/or safety, to reduce the burden of clinical trial assessments on patients. An example from the panel included the need for an endoscopy with small-intestine biopsy both at baseline and end of treatment to show histologic improvement in the underlying disease. Early phase, noninvasive markers may eventually be useful to identify a biological process or response to treatment for use in clinical trials. However, such markers that reliably reflect the underlying disease process or response to treatment have not yet been identified as a replacement of histologic assessment in clinical trials evaluating therapies for celiac disease.

One of the struggles researchers face is figuring out how celiac disease compares with other gastrointestinal diseases that have drugs for treatment. Clinical trial designs must take into consideration the differences between celiac disease and other gastrointestinal diseases. Often, celiac disease trials require a new design because they cannot be based on previous trials of other gastrointestinal diseases. When the trial's design is different and has less precedent, it becomes more challenging to clinically predict how the trial will turn out. Additionally, it's less clear how patients, health insurance companies and the FDA are going to accept the drug. Panelists said we need an understanding of the best practices of celiac disease clinical trials to overcome this barrier.

Lack of full understanding of which symptoms reported by celiac disease patients are caused by gluten is another hindrance, a panel member noted. Identification of the symptoms that a celiac disease therapy should treat and that can then be used as endpoints in a clinical trial is also needed. In one study, nausea and vomiting were symptoms reported by participants as opposed to diarrhea and abdominal pain.[6] Diarrhea and abdominal pain are often associated

[2] https://doi.org/10.1093/ajcn/85.1.160
[3] https://www.ncbi.nlm.nih.gov/pubmed/17382600
[4] https://www.ncbi.nlm.nih.gov/pubmed/24980880
[5] https://www.ncbi.nlm.nih.gov/pubmed/30769836
[6] https://www.ncbi.nlm.nih.gov/pubmed/31769533

with gluten exposure in celiac disease patients and consequently were used as endpoints in the clinical trial, but nausea and vomiting were not included as endpoints. More information about the symptoms caused by exposure to gluten alone, without other ingredients such as FODMAPs that could cause other symptoms, is needed.

Panelists noted that failed trials can provide valuable information that can inform future clinical trials. Additionally, the panel said there is a need to connect the dots between biomarkers, including T-cell response, biopsy results and symptoms, with proof that improvement in one will lead to improvement in all as the ultimate goal. At this time, establishing a correlation between biomarkers, histology, and/or symptoms, etc., is not an expectation for clinical trials. Some celiac disease patients have a stronger interest in a treatment that would protect against cross-contact than in a cure. A 2016 study found that 87 percent of patients surveyed were interested in a drug they could take in addition to a diet, compared to 65 percent interested in one that would replace the diet.[7]

Additionally, a Beyond Celiac and Canadian Celiac Association survey of celiac disease patients and parents of children who have celiac disease done in advance of the summit found that nearly 64 percent are willing to participate in a clinical trial, but are most hesitant about gluten challenge and biopsies as part of a study.[8]

Panelists agreed that lack of funding is a major barrier to advancing celiac disease research.

The FDA perspective

Clinical benefit on a meaningful aspect of how patients feel, function or survive as a result of treatment are key ways in which the FDA assesses response in clinical trials, according to the panel of FDA representatives. Additionally, clinical benefit must be meaningful, measurable and interpretable.

One challenge in celiac disease is defining the target population of interest for enrollment in clinical trials. Signs and symptoms of celiac disease vary among patients and can overlap with other diseases. To address this dilemma, researchers need to be sure that study participants have a diagnosis of celiac disease, confirmed by histology, and that symptoms, if present, are related to active celiac disease. Researchers need tools to measure relevant signs and symptoms that, if improved, would represent a clinical benefit, and they should determine what degree of improvement would provide convincing evidence patients have benefited from treatment. Representatives emphasized that clinical trials evaluating therapies intended to treat celiac disease should be designed to evaluate a drug's effect on both the underlying disease (e.g., histology) and signs and symptoms that result from gluten exposure.

The impact of the Hawthorne effect, in which patients who know they are being observed become more adherent to their gluten-free diet while participating in a study, was also

[7] https://www.ncbi.nlm.nih.gov/pubmed/27405659
[8] https://www.beyondceliac.org/research-news/celiac-disease-patients-willing-to-participate-in-most-studies-survey-finds/

discussed as a potential challenge during clinical trials, since patients are asked to maintain a daily diary documenting all food intake during the clinical trial. The FDA acknowledged that this phenomenon could influence the outcomes of clinical trials evaluating patients with celiac disease, and that methods to minimize bias, while collecting relevant information, should be considered when designing clinical trials.

FDA representatives emphasized the importance of stakeholder collaboration, including patients, advocacy groups, researchers and pharmaceutical companies, to inform drug development for celiac disease. Previously the FDA has brought together stakeholders to publicly discuss endpoints and advancement of therapies, most recently in the Gastroenterology Regulatory Endpoints and the Advancement of Therapeutics (GREAT) 3 Workshop.[9] In addition, the patient experience is increasingly being incorporated into decisions for drug development programs. The FDA encourages patient input during planning of clinical trials and for the selection or development of clinical outcome assessment tools that are intended to measure relevant signs and symptoms of celiac disease.

The payer perspective

The summit was one of the few stakeholder meetings to include a participant representing the payer perspective. Lack of broad communication between health insurance company representatives and other stakeholders might help explain why payers do not fully understand the unmet need for new therapies in celiac disease. Even with FDA approval, a drug will have difficulty getting to patients if payers cannot see the value in new therapies as opposed to the gluten-free diet.

The payer representative at the summit noted that the science that demonstrates that a medication is effective is necessary to get payers, as well as the medical community, onboard. Some considerations include: is the drug the only one to treat the disease; if not, how does it compare to other drugs or treatments in cost and effectiveness; how prevalent is the disease the drug is designed to treat and how will that determine use of the medication or treatment?

Payers will look at how any new drug compares to the standard of care that already exists. In the case of celiac disease, the gluten-free diet, which is often considered effective, will be considered standard of care. A new celiac disease treatment would be compared to the standard of care, whether it's used in addition to or as a replacement for the gluten-free diet. Side effects from any drug will have to be weighed against the severity of symptoms.

Other considerations are whether upfront drug costs might avoid downstream healthcare costs. In relationship to celiac disease, that would mean looking at the cost of long-term complications of the disease in quality of life and use of healthcare resources. In addition, lost days at work and school could be considered.

[9] https://www.gastrojournal.org/article/S0016-5085(16)34821-1/fulltext?referrer=https%3A%2F%2Fwww.ncbi.nlm.nih.gov%2F

How and whether to include children in clinical trials

Pediatric celiac disease experts who formed a panel to discuss the inclusion of children in clinical trials made a case for paying more attention to this often neglected area of celiac disease research. Including adolescents in adult clinical trials could be a first step toward filling the pediatric gap, the panelists concluded.

Adolescents were identified as a group that stands to benefit from clinical trials, can assent to participation, and comprehend trial protocols and procedures.

Some considerations that might allow for adolescents to participate in a clinical trial include whether: the disease is sufficiently similar for both adolescent and adult patients; the appropriate endpoints of the clinical trial to assess clinical benefit are similar; and the safety of the treatment is known or assumed to be similar.

Additionally, the panel pointed out some advantages and opportunities for younger children to participate in clinical trials. While parental concern about involving a child in a clinical trial is great, parents also have anxiety about whether the gluten-free diet and the way they are managing it daily is really protecting their child from the consequences of celiac disease. A safety net provided by a drug or therapy could be attractive to parents and drive participation by children, a panelist noted.

There are specific considerations to designing pediatric clinical trials, depending on the age group of the enrolled patients. For example, while young children are likely to have better adherence to the gluten-free diet compared to adolescents, adolescents can self-report on study questionnaires compared to young children, whose responses have to come through an observer, usually a parent. Both dietary adherence and self-reporting are components of many celiac disease trials.

The type of study being done can also influence the type of pediatric population most suitable for trial participation, for example whether a trial was designed to test a drug that would be used in addition to the gluten-free diet or if the drug would replace the gluten-free diet. An immunological-based therapy would have to take into consideration that the immune system of young children is different from the system of adolescents and adults, according to the panel.

The role of patient advocacy groups in getting therapies to patients

An international panel of celiac disease advocacy groups, including representatives from the United States, Canada and the United Kingdom, pointed to their role in funding research as critical to advancing new therapies.

This includes encouraging young investigators and supporting ongoing studies. Additionally, advocacy groups can accelerate new treatments by educating celiac disease patients about the importance of their role in research and how clinical trials and other types of research work. The

groups also play a key role in keeping patients and caregivers engaged and up-to-date on drugs in development and other celiac disease research.

Advocacy groups could also take the lead in bringing together appropriate stakeholders to advance the next steps outlined at the summit.

Action items identified at the summit

The panel presentations were followed by a strategy session where summit participants proposed action items. Fifteen actions were identified at the Summit that will help overcome the barriers remaining to bringing treatments to market. They are listed below in four broad categories. Participants noted that follow-up meetings among stakeholders will be necessary to further develop these action items and to identify additional action items. Discussion of next steps and assignments of working groups will continue over the next 4-6 months.

Celiac disease awareness and education

- *Re-evaluate the way patients are educated about the gluten-free diet.* Newly diagnosed patients are often presented with the message that the diet is a simple and complete treatment. While this approach seeks to help the newly diagnosed patient, it minimizes the burden of the disease. Summit participants noted that this approach is a barrier to getting patients to be willing to participate in clinical trials. New messaging to reassure gluten-free diet adherent patients who are still symptomatic that despite their best efforts gluten exposure can still occur and complete intestinal healing does not always occur. Studies show that up to 30% of patients continue to have symptoms while following the diet.[10] Information that the diet is not a complete treatment can be shared without discouraging patients from following the diet, which is still the only treatment available.

  This new education can be carried out by physicians diagnosing patients, by dietitians providing nutritional counseling, and by patient advocacy groups, who provide resources to guide people with celiac disease.

- *Emphasize the need for follow-up care*. Previous research from Beyond Celiac shows that more than one in four patients don't receive follow-up care.[11] Other research also shows that many patients do not get appropriate follow-up care.[12] On-going follow-up care would result in closer monitoring of celiac disease, including blood, urine and stool tests to determine when gluten exposure is occurring. Regular nutritional consultations with a dietitian may also be needed.

  This could be accomplished through the education of primary care physicians, gastroenterologists, and as part of ongoing patient education by patient advocacy groups.

[10] https://www.ncbi.nlm.nih.gov/pubmed/25662623
[11] https://bmcgastroenterol.biomedcentral.com/articles/10.1186/s12876-017-0713-7
[12] https://www.ncbi.nlm.nih.gov/pubmed/30597204

- *Encourage patients to participate in clinical trials*. Advocacy groups can present clinical trials and information about research to the patient community. This can include information about ongoing clinical trials patients may qualify for and results of completed clinical trials.

  Electronic health records could trigger a note to physicians to bring up clinical research as a care option when a diagnosis is made, and laboratory systems set up to give notification of positive celiac disease test results, initiatives that could be led by physicians and healthcare systems.

Medical care and research needs

- *Create a celiac disease passport* that would be given to each patient at diagnosis and would be available to patients and anyone to whom they give access. The passport would confidentially track all patient information and changes, including record of diagnosis and any follow-up care. Primary care physicians and gastroenterologists would be encouraged to offer it to patients. Patients who want to participate in clinical trials and have to show medical documentation of their diagnosis could do so through the passport. This could be a collaborative effort between patient advocacy groups and researchers.

- *Evaluate and describe the true economic impact of celiac disease*. Funding is needed for a well-designed study on a macroscale of populations with celiac disease and the impact on healthcare utilization and on a microscale with granular data on actual cost of having celiac disease and could include information on missed work and school. This economic impact data could be used to support the need for alternate or additional treatments for celiac disease and could be helpful for payers.

- *Identify early predictive markers* of a potential treatment's relevance in celiac disease through a request for applications put out by patient advocacy groups or other funding sources. This could help speed the search process for new potential molecules that will have an impact on the immune response triggered by gluten.

- *Quantify real-life gluten exposure for celiac disease patients following a gluten-free diet.* It is not realistic to eat a diet 100 percent free of gluten because even foods labeled "gluten-free" are allowed to contain < 20 parts per million of gluten. However, it is not clear how much gluten people with celiac disease are consuming on a daily basis. Once real-life exposure is quantified, it can be mimicked in clinical trials to demonstrate efficacy. Advocacy groups and celiac disease research centers could fund research specifically for ways to measure and mimic real-life exposure. For example, studies using urine and stool tests are attempting to measure gluten exposure in adults and adolescents.

Funding challenges

- *Develop methods to advocate for public funding for research and clinical trials.* Currently public funding goes broadly to immunology but needs a specific celiac disease focus. There is a need to drive home the necessity of having the NIH publicly fund the research that will actually bring treatments to patients. Patient advocacy groups can start the conversation with the NIH and engage people with celiac disease to advocate with Congress. A broader push from patients, pharmaceutical companies, researchers, and physicians is most likely needed to make this a true NIH priority.

- *Explore other ways of financing celiac disease research* aside from public funding. Patient advocacy groups are currently offering celiac disease specific funding, and more is needed. If there is to be more funding specifically for celiac disease, then celiac disease advocacy groups, academic research centers, and pharmaceutical companies may need to identify innovative ways to obtain that funding. Approaches could include venture philanthropy, a model used by the Cystic Fibrosis Foundation with great success.

Clinical trials

Pre-trial issues

- *Identify relevant disease markers and additional outcome measures for clinical trials.* The FDA has provided advice to individual drug companies when asked about endpoints for clinical trials. To date, most trials have relied on either change in histologic findings, as shown on a duodenal biopsy, and/or change in patient-reported outcomes centered on gastrointestinal celiac disease symptoms. There are many non-gastrointestinal symptoms of celiac disease that are not measured in clinical trials but are important to patients.[13] Researchers, patients, the FDA, and pharmaceutical companies can collaborate on this project.

- *Include the patient voice in the earliest part of the drug development process*. Through the Prescription Drug User Fee Act (PDUFA) VI and the 21st Century Cures Act, the FDA has provided basic guidance on involving patients in all phases of drug development. Patient involvement is crucial to ensure that developed therapies meet the needs of patients, and clinical trials are designed with patients in mind and endpoints that matter to them. Patient advocacy groups can help bring the patient voice to the process, and pharmaceutical companies need to create opportunities for patient involvement.

- *Develop guidelines for participants and trial providers*. When a trial is completed, participants should have access to information about their role in the trial, including

[13] https://www.beyondceliac.org/research-news/brain-fog-study-presented-at-international-celiac-disease-symposium/

whether they received treatment or placebo, the overall outcome of the trial, and access to any personal health record generated by their trial participation. There may be legal limits to what can be shared with participants. Researchers should put their best efforts into designing patient-centered trials that are less disruptive to participants' daily lives, including considering overall number of visits, travel time, and transportation convenience. Additionally, Summit participants noted they would appreciate a more palatable gluten challenge. Participants should be provided with clear expectations around how much they can share about their role in the trial.

Trial Execution

- *Standardize the gluten challenge*. This standardized challenge could be accessed by all researchers and pharmaceutical companies and the results of gluten challenges could be compared. This would lead to established expectations such as what symptoms arise from gluten consumption and the immune response following a gluten challenge. A standardized challenge would make clinical trials more consistent and comparable.

- *Include the pediatric celiac disease population in clinical trials.* Explore possible inclusion of adolescents in appropriate adult trials, and design trials that could safely include younger children. This would involve working with pediatric celiac disease centers.

Post-trial

- *Encourage researchers to consistently publish study results regardless of trial outcome*. Maximize the value of clinical research by making the raw data available after the first set of publications have been provided. This allows each trial to provide more information to the wider celiac disease research community. Researchers must take a non-competitive approach to achieve this goal.

Beyond Celiac Next Steps

Beyond Celiac conducted a post-summit analysis to determine key action items for a patient advocacy group to incorporate in its 2020 Science Plan and beyond. In addition to taking a leadership role in partnering and ensuring that appropriate stakeholders fulfill these action items, we can have the most impact in the following areas:

Celiac disease awareness and education: Our rebrand in 2016 brought a focus on research into treatments beyond the gluten-free diet. We have been educating the celiac disease community about the burden of the disease and research that shows limitations of the gluten-free diet, including the fact that symptoms still occur and intestinal healing is not complete. We will continue with this strong messaging by keeping patient education about research at the forefront of our activities. Through our Research News, we educate the celiac disease community about the latest advances in research. We will build on our previous Research

Symposiums, which focused on the need for patient participation in clinical trials, in innovative and newly engaging ways in 2020 and beyond.

Furthermore, through *Go Beyond Celiac*, our patient database, we have identified more than 6000 people with celiac disease who are willing to participate in research. Through our mobile app and website, we can communicate with this community very actively through insights and updates specifically designed to keep *Go Beyond Celiac* members engaged. We also plan to use this database for targeted clinical trial recruitment, in addition to the other methods we use for more general recruitment.

Clinical Trials: As the leading voice of the celiac disease community, Beyond Celiac will continue to represent the community to the FDA, drug developers, payers and other stakeholders. Our *Go Beyond Celiac* database and our connection with the community make us uniquely poised to answer questions about what it is truly like to live with celiac disease. We will continue to make sure the burden of celiac disease is not overlooked by these groups.

Furthermore, we will work to develop best practices for celiac disease clinical trials, including better communication with participants, making trials participant-friendly, and publishing trial results regardless of outcomes. We will continue to make the patient voice heard in all stages of drug development.

Funding Challenges: In 2019, Beyond Celiac awarded almost $600,000 in celiac disease research funding. We will continue to fund celiac disease research in identified priority areas and will take into consideration the topics identified at the summit as most critical to getting a treatment to patients. Our commitment is to fund grants that directly accelerate these efforts, as well as contribute to the advancement of celiac disease research overall.

Appendix 1: 2019 Beyond Celiac Research Summit Attendees

Bob Anderson, PhD
Celiac disease researcher

Jen Arters
Diagnosed with celiac disease

Kate Avery, MPH
Director of Research and Patient Engagement
Beyond Celiac

Claire Baker
Director of Communications
Beyond Celiac
Diagnosed with celiac disease

Alice Bast
President & CEO
Beyond Celiac
Diagnosed with celiac disease

Bob Beall, PhD
Executive Advisor
Cystic Fibrosis Foundation
Beyond Celiac Board of Directors and
Scientific Advisory Council

Deneen Bowlin, MD
Medical Director
CareFirst BCBSMD

Michael Boyne, PhD
Vice President of Product Development and Analytics
Cour Pharma

Jackson Buttery
Digital Content Coordinator
Beyond Celiac
Diagnosed with celiac disease

Priyanka Chugh, MD, MS
General Surgery Resident
Boston Medical Center

Diagnosed with celiac disease

Allan Coukell
Parent of child with celiac disease

Hilary Croft*[14]
Chief Executive Officer
Coeliac UK
Parent of child with celiac disease

Natalie Dabrowski
Parent of child with celiac disease

Meghan Donnelly, MS, RDN
Medical Affairs, Clinical Dietitian
Dr. Schar USA

Patti Goldberg
Grandparent of child with celiac disease

Sam Goldberg,MD
Grandparent of child with celiac disease

Laura Gordon
Chief Executive Officer
I-ACT for Children
Diagnosed with celiac disease

Kristie Grebe, PhD
Senior Director, Clinical & Translational Development
Anokion

Ann Horsburgh
Diagnosed with celiac disease

Doug Jacobstein, MD
Vice President, Clinical Development
Provention Bio

Julie Kennedy, MPH, MEd, RDN, LDN
Julie Kennedy Nutrition, LLC
Diagnosed with celiac disease

[14] * Views communicated in abstentia

Parent of child with celiac disease

Katie Kenyon
Diagnosed with celiac disease

Katelyn Koons
Diagnosed with celiac disease

Bruno Larida
Vice President – Country Manager
AESKU.INC

Irena Lavine, MD
Medical Officer
Division of Gastroenterology
Center for Drug Evaluation Research, FDA

Benjamin Lebwohl, MD, MS
Assistant Professor of Medicine and Epidemiology
Director of Clinical Research
Celiac Disease Center
Columbia University

Anne Lee, EdD, RDN, LD
Assistant Professor of Nutritional Medicine
Celiac Disease Center
Columbia University
Diagnosed with celiac disease

Dan Leffler, MD, MS
Medical Director
Takeda Pharmaceuticals
Associate Professor of Medicine
Harvard Medical School
Beyond Celiac Scientific Advisory Council

Aaron Lerner, MD
AESKU.KIPP Institute

Beth Llewellyn
Clinical Operations Consultant
Provention Bio

Maria Luci

Assistant Director of Digital Media
Beyond Celiac

Daniel Mallon, MD, MSHPEd
Pediatric Gastroenterologist
Assistant Program Director
Pediatric Residency Program
Cincinnati Children's Hospital

Ellen McKinley
Diagnosed with celiac disease

Steve Miller, PhD
Directory of the Interdepartmental Immunology Center
Judy Gugenheim Research Professor of Microbiology-Immunology
Northwestern University Feinberg School of Medicine
Beyond Celiac Scientific Advisory Council

Joe Murray, MD
Professor of Medicine
Gastroenterologist
Division of Gastroenterology and Hepatology
Mayo Clinic
Beyond Celiac Scientific Advisory Council

Ioannis Petrakis, MPharm, Msc, MPH, PhD
Global Head, GI Payer Value and Patient Access
Takeda Pharmaceuticals

Tina Ramos
Diagnosed with celiac disease

Amy Ratner
Medical & Science News Analyst
Beyond Celiac
Parent of child with celiac disease

Marie Robert, MD
Chief Scientific Officer
Beyond Celiac
Professor of Pathology
Yale School of Medicine

Roz Schneider, MD, MSC

Principal
RozMD Patient Affairs Consulting, LLC

Jennifer Sealey-Voyksner, PhD
Chief Scientific Officer
Director of Regulatory and Compliance
ImmunogenX
Diagnosed with celiac disease

Melissa Secord, CAE
Executive Director
Canadian Celiac Association

Jocelyn Silvester, MD, PhD
Assistant Professor of Pediatrics
Director of Research
Celiac Disease Program
Boston Children's Hospital

Michele Snyder
Clinical Operations
Provention Bio

Amelie Therrien, MD, MS
Clinical Fellow in Celiac Disease
Beth Israel Deaconess Medical Center, Harvard
Diagnosed with celiac disease

Juli Tomaino, MD, MS
Lead Medical Officer
Division of Gastroenterology
Center for Drug Evaluation Research, FDA

Ritu Verma, MD
Medical Director
University of Chicago Celiac Center
Beyond Celiac Board of Directors
Parent of children with celiac disease

Table 1

Stakeholder Reported Barriers to Celiac Disease Therapies		
Patients and Advocacy Groups	**Pharmaceutical Industry, Regulators and Payers**	**Pediatric and Adult Physicians and Scientists**
Ongoing confusion on diagnostic criteria for celiac disease	Limited funding for R&D of potential therapies for celiac disease	Lack of inclusion of children and their special needs, from early childhood through adolescence in the discussion of celiac therapies
Societal perception that celiac disease is not a real disease	Challenges of clinical trial recruitment of this patient population, especially when gluten challenge is needed	Lack of education of pediatric gastroenterologists on clinical trial access, especially for adolescent age group
Lack of patient and clinician education on need for therapies beyond the gluten-free diet	Need for additional clinically meaningful endpoints	Overreliance on symptoms to determine response to either diet or therapies
Entrenched belief that the gluten-free diet is a complete treatment, bolstered by social media	Lack of precedent for path to drug approval by FDA as there are no approved pharmacologic therapies at this time	Lack of objective biomarkers to measure disease activity in celiac disease
Distrust that gluten could ever be safe, even with therapies Fear of research and medicine	Regulatory challenges for trial design in face of existence of gluten-free diet and varying definitions of successful endpoints	Diverging research strategies aimed at either tolerance induction or symptom reduction
Uncertainty of the risk/benefit of taking medicine long term, despite high burden of gluten-free diet	Concern for market access, need for definitions of target populations for treatment, and payer buy-in to cover costs	Need for basic and translational science funding to uncover additional targetable T-cell epitopes responsible for inflammatory response in celiac disease