



**CORPORATE PRESENTATION**  
(NASDAQ:ENTO)

***Targeted, Non-Systemic Therapeutics for Gastrointestinal Diseases***

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- **First Wave BioPharma Merger with ImmunogenX**
- **Business Combination Creates A Best-In-Class, Late-Stage Pipeline of Targeted, Non-Systemic Therapeutics for Gastrointestinal Diseases**
- **Latiglutenase Therapeutic for Celiac Disease to be Advanced to Phase 3 Clinical Trial**

(NASDAQ:ENTO)

# Entero Therapeutics: A Merger of First Wave and ImmunogenX

## Focused on GI Indications

### ▪ **Business Combination: Strong Strategic Fit**

- First Wave BioPharma (NASDAQ:FWBI) and privately-held ImmunogenX (IMGX)
- GI pipeline expansion into Celiac Disease with a Phase 3-ready asset
- Merged company has four gut-targeted, late-stage GI assets
- Robust pipeline to address key unmet medical needs afflicting millions of patients in multi-billion dollar markets

### ▪ **Transaction**

- 100% equity transaction
- Non-binding commitment for significant financial investment from a strategic biopharmaceutical company in exchange for commercial rights to latiglutenase
- Potential financing commitments from several institutional investors

### ▪ **Synergistic Integration of Management Teams**

- FWBI: Operational, financial and commercial expertise
- IMGX: Scientific, clinical and regulatory affairs expertise
- Core competence in development of recombinant digestive enzymes

## Overview: GI Company with multiple late-stage clinical assets

**Entero Therapeutics** is a clinical stage biotechnology company currently focused on the development of targeted, non-systemic therapies for gastrointestinal diseases

### LATIGLUTENASE

#### **Recombinant enzyme; dual-protease biologic for the treatment of Celiac Disease (CeD)**

- Targeting symptom relief and quality of life (QOL) improvements
- Phase 3 clinical trial initiation anticipated in 2025

### CAPESEROD

#### **Re-purposed selective 5-HT4 receptor partial agonist for gastrointestinal indications, including gastroparesis**

- Asset in-licensed from Sanofi
- Phase 2 Gastroparesis trial initiation anticipated in 2025

### ADRULIPASE

#### **Recombinant enzyme; lipase biologic for the treatment of Exocrine Pancreatic Insufficiency (EPI)**

- EPI in Cystic Fibrosis (CF) and Chronic Pancreatitis (CP)
- Phase 2 Bridging Study topline data 2H'23; FDA Type-C meeting to be requested 1H'24

**Robust IP portfolio covering method, formulation and use indications; key patents secure for 15-20 years**

**Pipeline of gut-targeted GI therapies address significant unmet medical needs in billion-dollar markets**

# Entero Therapeutics Management Team

Combined Experience in Developing and Launching more than 25 Drugs



**James Sapirstein**

Chairman & Chief Executive Officer



**Jack Syage, Ph.D.**

President & Chief Scientific Officer



**Sarah Romano**

Chief Financial Officer



**Martin Krusin**

SVP Corporate Development



Immunogen<sup>®</sup>



SYAGEN



SAFRAN

Caltech

- Led Gilead's launch of Tenofovir/ Viread
- Director of BMS International Infectious Disease Group
- Founder of Tobira, sold to Allergan for \$1.7B

- Serial entrepreneur, closed four acquisitions
- >30 years developing innovative technologies
- 140 publications, 80 invited talks, 30 U.S. patents, Fellow of the American Physical Society, Tibbetts Award (SBIR), OC 500

# Entero GI Clinical Pipeline (2023-2028)

	Indications	2023	2024	2025	2026	2027	2028
<b>Latiglutenase</b>	• Celiac Disease			Phase 3 Dosing	Phase 3 Safety	★	BLA
<b>Capeserod</b>	• Gastroparesis			Phase 2*			
<b>Adrulipase</b>	• EPI in CF • EPI in CP	Phase 2b					
<b>Nicosamide**</b>	• Multiple Phase 2 Indications***	All Indications Phase 2 ready					

\* Subject to FDA IND review

\*\* A non-binding term sheet has been signed for the sale of Nicosamide

\*\*\* Ulcerative Proctitis/Proctosigmoiditis, Ulcerative Colitis, ICI-AC, Pouchitis, Crohn's Disease



# LATIGLUTENASE

Celiac Disease



## Latiglutenase: A First-to Market Opportunity in Celiac Disease

- Latiglutenase, a targeted Celiac Disease therapeutic to provide symptom relief and Quality of Life improvements, with first-to-market opportunity
- Addressing an unmet clinical need in a multi-billion dollar market, there are no commercially available therapies for Celiac Disease
- Compelling endpoint data from Phase 2 trials and solid FDA support
  - Strong Peer Review Support - \$7.7MM in NIH grants
  - FDA Successful End-of-Phase 2 Meeting completed
  - FDA Support for Phase 3 Trial Endpoints and Fast Track Designation
  - FDA Agrees with Initial Pediatric Study Plan
- Phase 3 Trial initiation anticipated 1H'2025; market entry 2H'2027

# Celiac Disease (CeD)

## Large Unmet Need, No Therapies Available

- Genetically predisposed autoimmune disease caused by eating gluten; a protein found in wheat, barley, and rye
  - ~1% of the world's population<sup>1</sup>
  - ~3.3 million patients in the US alone
- Chronic and debilitating gastrointestinal problems and other long-term health issues
- Only current treatment is a gluten-free diet (GFD) which is impractical and often ineffective
- CeD patients typically consume 100's of mg/day of gluten where <50 mg/day is considered safe<sup>2</sup>
- Patients live in fear that a trace amount of gluten can unexpectedly trigger a painful and debilitating flare-up
  - 73% of CeD patients have exposure to gluten and symptoms once a year despite being on a GFD<sup>3</sup>
  - Nearly 40% of CeD patients reported accidentally ingesting gluten as often as 1-5 times month with over two-thirds having severe GI symptoms<sup>3</sup>



<sup>1</sup> P Singh, A Arora, Tor Strand, et al. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. Clinical Gastroenterology and Hepatology. March 15, 2018 DOI: <https://doi.org/10.1016/j.cgh.2017.06.03>

<sup>2</sup> J A Syage, C.P Kelly, M A Dickason, A Cebolla-Ramirez, F Leon, R Dominguez, J A Sealey-Voyksner, Determination of Gluten Consumption in Celiac Disease Patients on a Gluten-Free Diet. Am. J. Clin. Nutr., 107, 201-207 (2018)

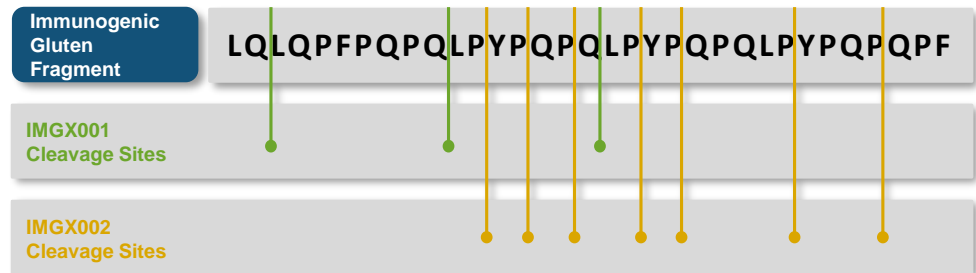
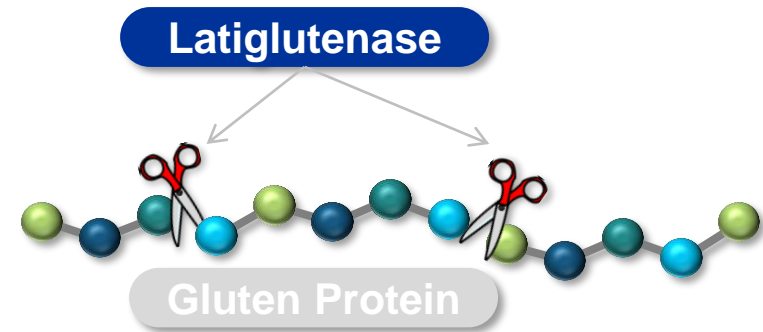
<sup>3</sup> <https://www.beyondceliac.org/ceeliac-news/73-percent-still-exposed-gluten/>

# Latiglutenase is a Potential Breakthrough Treatment

## Highly Differentiated Mechanism of Action

**Latiglutenase** is a non-systemic, orally-administered biologic enzyme treatment that degrades gluten

- Two recombinant gluten-specific enzymes (proteases) work together to break down the gluten protein in the stomach
- Gluten fragments are made too small (non-immunogenic peptides) to trigger the autoimmune response
- Safe, non-systemic drug
- It comes in a flavored powder form and is mixed together with water that CeD patients drink when eating food



## \$1.2 Billion Annual Market Seroactive\* Opportunity in Celiac Disease

- **FDA Label for Latiglutenase: Symptom Relief for Seroactive Patients**
  - Phase 2b and 3 primary endpoint: \$1.2B per year
  - 2035 projection for seroactive patients only:
    - 134,000 (US – 30% penetration)
    - 180,000 (EU – 18% penetration)
- **IP through 2039, with 12 years biologics exclusivity (U.S.), 10 years Europe**
- **Payor support for higher price points, CeD severity viewed as being comparable to Ulcerative Colitis and Crohn's Disease**

*\*Seroactive = positive for any of the antibodies (TTG-IgA, DGP-IgA, DGP-IgG) in a single blood test*

## Latiglutenase Phase 3 Plan – Alignment with FDA Established

- **Label: FDA recommends symptom reduction and histologic non-worsening in active symptomatic Celiac Disease**
- Dual (two replicate) 26-week Phase 3 efficacy trials with an additional 26-week safety run-out in symptom responders
- Efficacy endpoints (change from baseline to week 24)
  - **Primary: Non-stool GI (abdominal pain, bloating, nausea) composite score reduction**
  - **Secondary: Histologic non-worsening as measured by VCIEL (Vh:Cd + IEL)**
- Two cohorts (placebo, 1200 mg)
- Stratify to:
  - **Seroactive, Vh:Cd < 1.8**
  - **Seroactive,  $1.8 \leq \text{Vh:Cd} \leq 2.8$**
- Total anticipated completed patients N = 640-800 (total for both Phase 3 studies)

All components of the Phase 3 Plan are agreed to by the FDA

- Type C Meeting (Aug 31, 2022) Minutes
- EOP2 Meeting (Apr 12, 2023) Minutes

Vh:Cd    Villous Height/Crypt Depth  
IEL    Intraepithelial Lymphocytes



## **CAPESEROD**

New GI Opportunity In-Licensed from Sanofi

## **ADRULIPASE**

Exocrine Pancreatic Insufficiency in  
Cystic Fibrosis & Chronic Pancreatitis

## Capeserod: Proprietary Mechanism of Action Applicable to New GI Indications

- Capeserod, a selective 5-HT<sub>4</sub> receptor partial agonist small molecule, was in-licensed from Sanofi in September 2023
- In previous Sanofi Phase 1 and Phase 2 CNS trials, involving over 600 patients, Capeserod appeared safe and well-tolerated
- Research on Capeserod and subsequent artificial intelligence (AI)-empowered analyses suggest that the drug possesses a mechanism of action that increases gastric motility that is applicable to several GI indications underserved by currently available therapeutics in multi-billion dollar markets.
- First Wave will repurpose Capeserod for gastrointestinal (GI) indications, and plans to initiate a Phase 2 gastroparesis clinical development program
- Sanofi retains the right of first refusal (ROFR) to develop and commercialize Capeserod

## Adrulipase: Exocrine Pancreatic Insufficiency (EPI)

A chronic nutritional deficiency – the pancreas is damaged and does not produce the digestive enzymes needed to break up food in the GI tract so that nutrients can be absorbed

### EPI related morbidities

- Poor fat absorption
- Unable to gain or retain weight
- Frequent bowel movements & diarrhea
- Abdominal discomfort and pain

### Focus on two patient populations requiring treatment for EPI

#### Cystic Fibrosis

##### Genetic disease

- ~40,000 patients U.S.,  
~100K-160K\* worldwide
- Treatment begins for patients in first six months of life

#### Chronic Pancreatitis

##### Heterogeneous disease

- ~95,000 patients U.S.,  
~450K-600K worldwide
- Alcoholism
- Pancreatic cancer
- Pancreatic surgery

Sources: Guo, J. Worldwide rates of diagnosis and effective treatment for cystic fibrosis, Journal of Cystic Fibrosis 21(2022) 456-462 – estimate of ~ 60K undiagnosed individuals with CF. Cystic Fibrosis Foundation 2023. The CorStar Group 2019.

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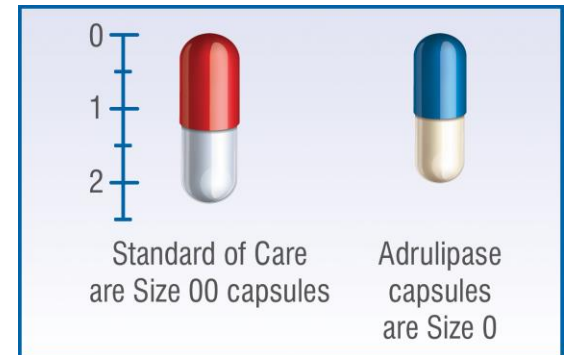
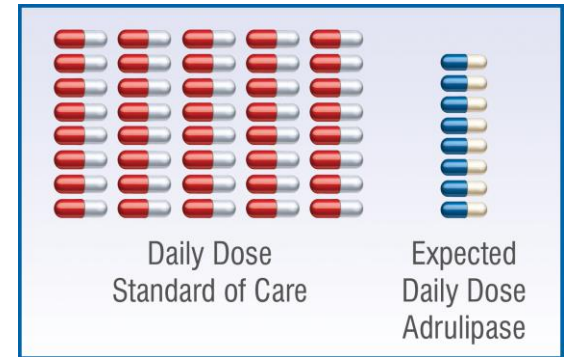
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# Adrulipase: Fulfilling an Unmet Medical Need

Large Established U.S. Market Of ~\$1.8 Billion (\$2.3B Global)

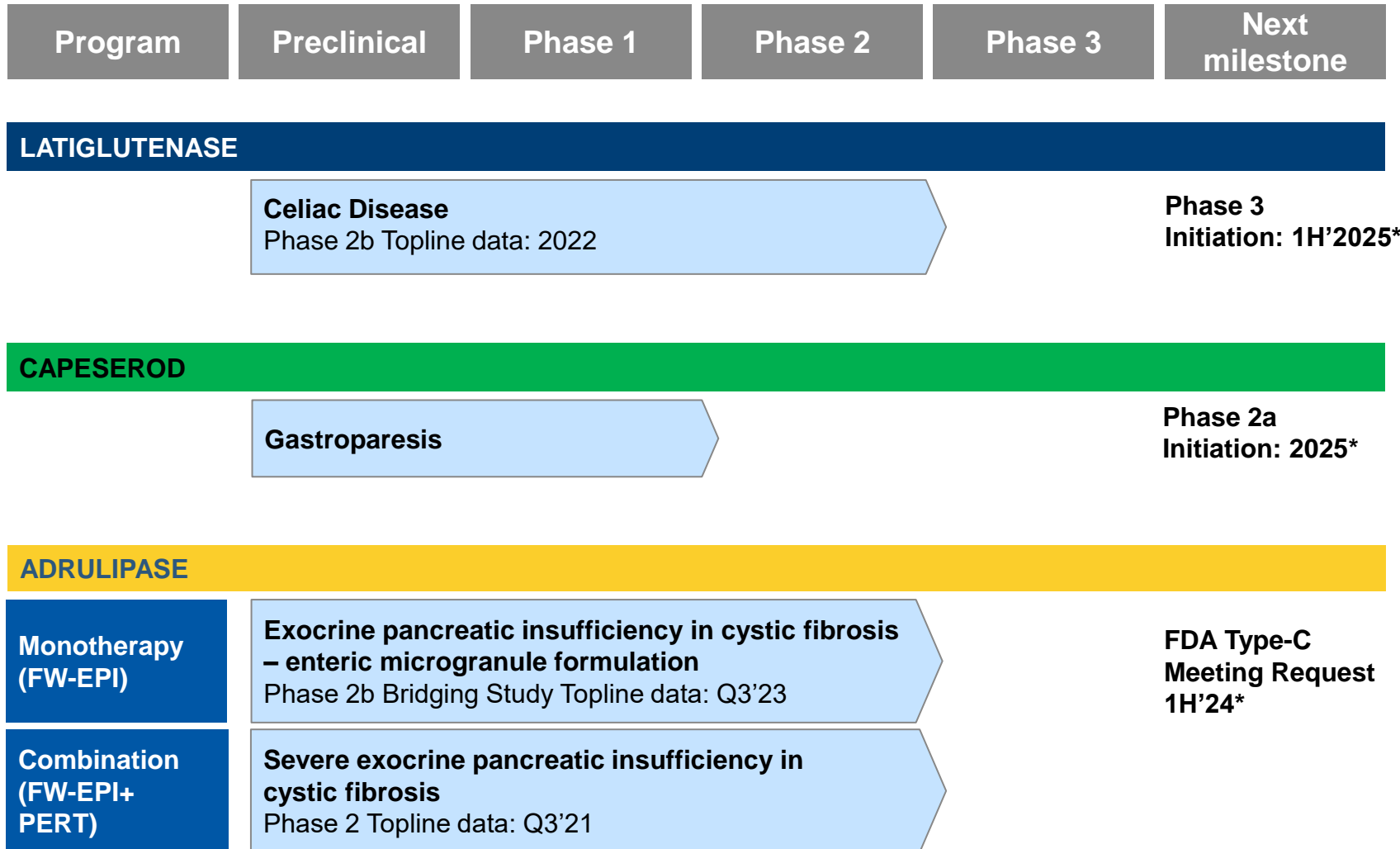
	PERT	ADRULIPASE
Drug Substance	<ul style="list-style-type: none"> <li>▪ <b>Porcine-derived</b> pancreatic enzyme replacement therapy (PERT)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Recombinant yeast</b> (<i>Yarrowia lipolytica</i>) lipase-derived replacement therapy</li> </ul>
Safety	<ul style="list-style-type: none"> <li>▪ <b>Adverse event: fibrosing colonopathy at high doses</b></li> <li>▪ FDA black box warning</li> <li>▪ ~30% of CF patients are not well controlled on PERT and cannot dose up</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Safe and well tolerated to date</b></li> <li>▪ No fibrosing colonopathy</li> <li>▪ No porcine allergies</li> </ul>
Pill Burden	<ul style="list-style-type: none"> <li>▪ <b>25-40 pills per day (CF)</b></li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>5-8 pills per day (CF)</b></li> </ul>
Sourcing & Supply	<ul style="list-style-type: none"> <li>▪ Subject to pig herd management</li> <li>▪ <b>Risk of transmission of animal pathogens</b></li> <li>▪ Manufacturing + supply chain inconsistency</li> </ul>	<ul style="list-style-type: none"> <li>▪ GRAS (Generally Regarded as Safe)</li> <li>▪ <b>No risk of animal pathogens</b></li> <li>▪ Manufacturing + supply chain consistency</li> </ul>



Differentiated mechanism of action | No dose-limiting safety issues to date on ~100 patients

Sources: Results from the Company's clinical trials, internal studies and management estimates.

# Three Therapeutic Assets: Multiple Phase 2 and 3 Clinical Indications



\* Anticipated

## CONTACT US

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