August 2023

CORPORATE PRESENTATION

(NASDAQ:FWBI)

Targeted, Non-Systemic Therapeutics for Gastrointestinal Diseases

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Overview
Two therapeutic assets and multiple Phase 2-ready clinical indications

First Wave BioPharma is a clinical stage biotechnology company currently focused on the development of targeted, non-systemic therapies for gastrointestinal diseases

ADRULIPASE	**Recombinant enzyme; lipase biologic for the treatment of Exocrine Pancreatic Insufficiency (EPI)** • EPI in Cystic Fibrosis (CF) and Chronic Pancreatitis (CP); new enteric microgranule formulation • Phase 2 Bridging Study initiated Jan. 2023, topline data 2H'23
NICLOSAMIDE	**Re-purposed small molecule drug with potent anti-inflammatory properties, proprietary micronized formulation** • IBD: Ulcerative Colitis-Ulcerative Proctitis • Immune Checkpoint Inhibitor-Associated Colitis

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

First Wave BioPharma Management Team

Combined Experience in Developing and Launching more than 25 Drugs

James Sapirstein
Chief Executive Officer

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

James Pennington, MD
Chief Medical Officer

- Led successful registration efforts for 12 BLA/NDA submissions in the U.S. and 10 in Europe and Asia
- 10 years on Harvard Medical School faculty

First Wave BioPharma

ADRULIPASE

FW-EPI: Exocrine Pancreatic Insufficiency in Cystic Fibrosis & Chronic Pancreatitis

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

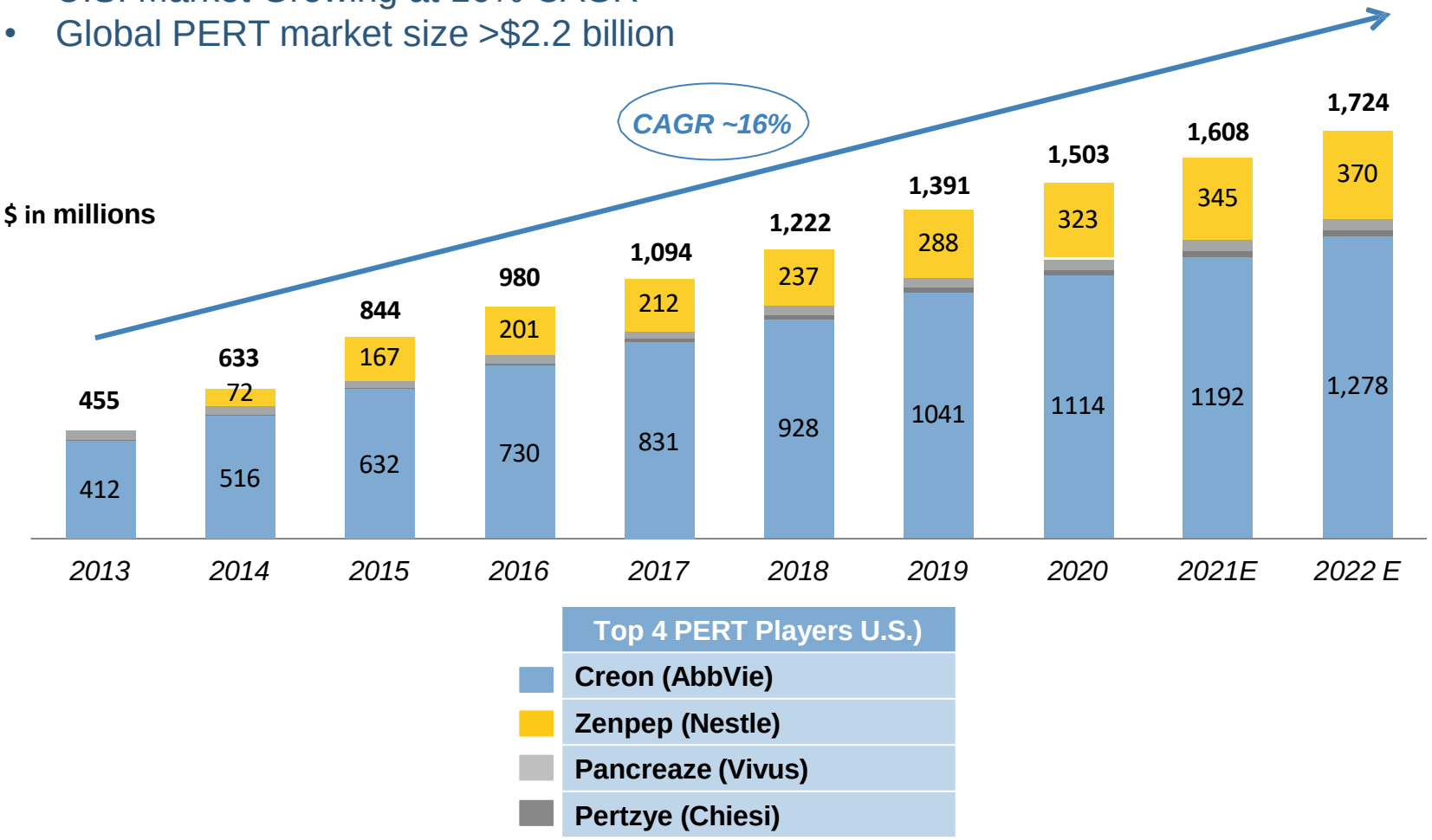
- **~95,000 patients U.S., ~450K-600K worldwide**
- Alcoholism
- Pancreatic cancer
- Pancreatic surgery

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.

Large Established U.S. Market Of ~$1.7 Billion(1)

All lipase products are pig derived and are less active at the pH in humans resulting in a large pill burden

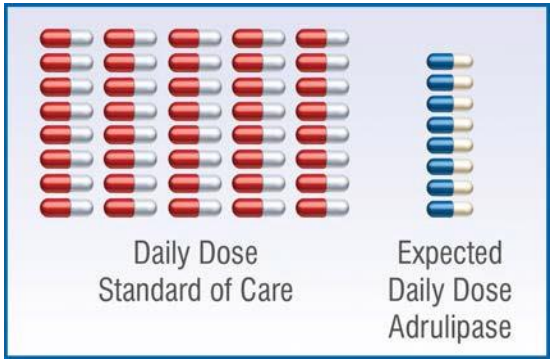
- U.S. Market Growing at 16% CAGR
- Global PERT market size >$2.2 billion

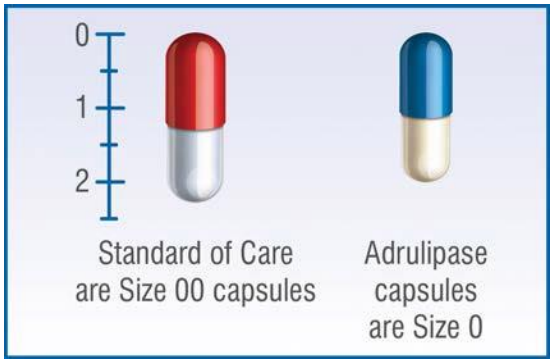


Sources: Global Market Size: Symphony Health 2019. The CorStar Group (2019). U.S. Market Size: Creon 2013-2023 AbbVie 10-K's, 2021 Mgmt. Estimate; Zenpep, Allergan 2014-2020 10-Ks, 2021 Mgmt. Estimate; Vivus and Pertzye.

Adrulipase: Fulfilling an Unmet Medical Need

	PERT	ADRULIPASE
Drug Substance	■ **Porcine-derived** pancreatic enzyme replacement therapy (PERT)	■ **Recombinant yeast** (*Yarrowia lipolytica*) lipase-derived replacement therapy
Safety	■ **Adverse event: fibrosing colonopathy at high doses** ■ FDA black box warning ■ ~30% of CF patients are not well controlled on PERT	■ **Safe and well tolerated to date** ■ No fibrosing colonopathy ■ No porcine allergies
Pill Burden	■ **25-40 pills per day (CF)**	■ **5-8 pills per day (CF)**
Sourcing & Supply	■ Subject to pig herd management ■ ***Risk of transmission of animal pathogens*** ■ Manufacturing + supply chain inconsistency	■ GRAS (Generally Regarded as Safe) ■ ***No risk of animal pathogens*** ■ Manufacturing + supply chain consistency





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.

Adrulipase Clinical Trial Efficacy Endpoints
Pursuing a Non-Inferiority Pathway

Primary Efficacy Endpoint	
Coefficient of Fat Absorption (CFA)	≥80%

Secondary Efficacy Endpoints
• Stool Consistency (Bristol Scale)
• Stool Quantity (Weight)
• Bowel Movements
• Steatorrhea
• Abdominal Discomfort (Visual Analog Scale)
• Weight Gain
• BMI
• Coefficient of Nitrogen Absorption (CNA)

Lessons Learned From the Adrulipase Program and Next Steps

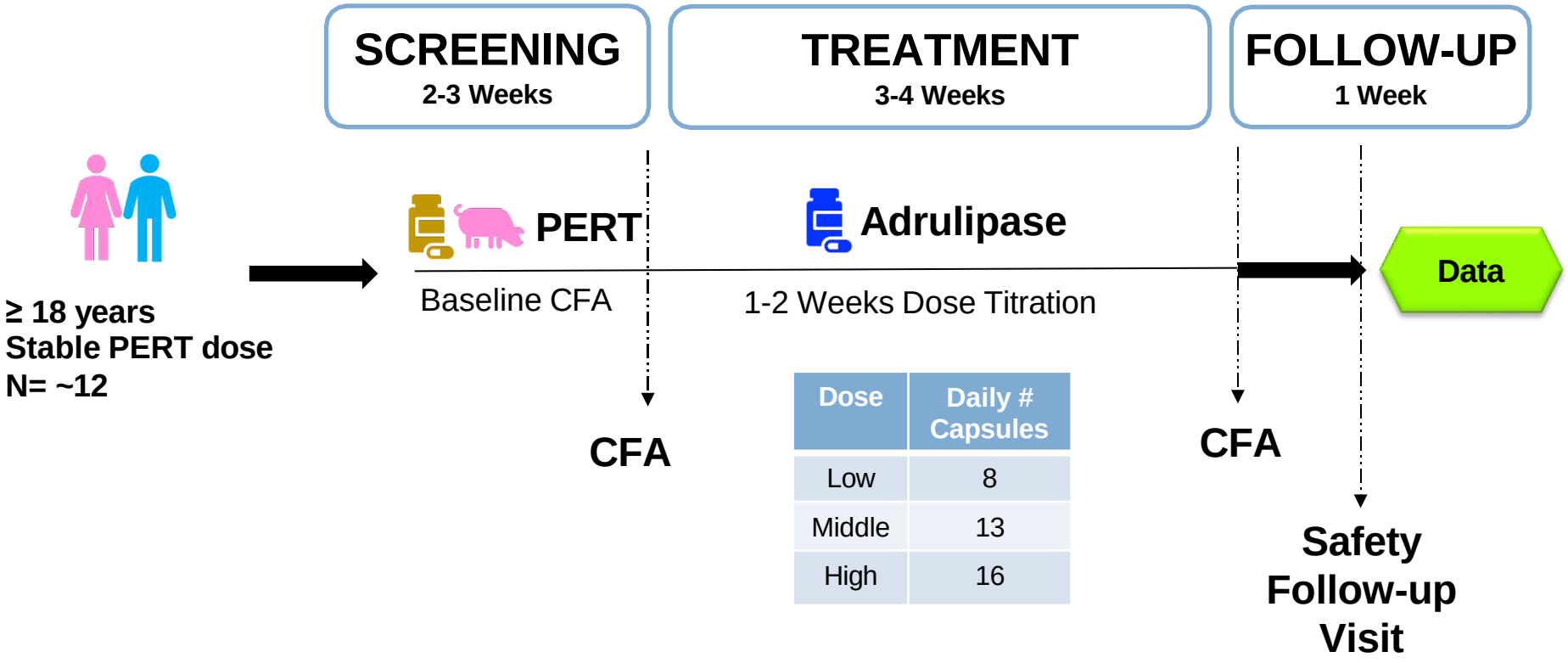
- **Four Phase 2 Studies**
  - Cystic Fibrosis & Chronic Pancreatitis
  - Monotherapy & Combination Therapy
- Product has evidence of lipase activity
- Product shows dose-response in chronic pancreatitis
- Combination therapy with PERT shows clinically meaningful improvement for less controlled patients with Severe EPI in cystic fibrosis
- Safety is excellent at all doses studied
- Despite lack of protease, CNAs are consistently >80%
- Powder formulation in immediate release or enteric capsules was not sufficient to obtain consistent CFAs >80%
- Formulation with good gastric dispersion plus gastric acid protection logical next step

- 2020-2022: Enteric Microgranule Formulation Development
- 2023: Phase 2 Adrulipase Bridging Study with new Formulation Initiated

Adrulipase Phase 2 SPAN Bridging Study

Trial Initiated Jan. 2023, Topline Data Anticipated July 2023

A Phase 2, Open Label, Multicenter, Pilot Study to Assess Safety and Efficacy of an Enteric Microgranule Formulation of Adrulipase in Patients with Exocrine Pancreatic Insufficiency (EPI) due to Cystic Fibrosis (CF)



Dose	Daily # Capsules
Low	8
Middle	13
High	16

Adrulipase Summary

- Targeting patients with **Cystic Fibrosis (CF)** and **Chronic Pancreatitis (CP)**
- Addressing an established PERT global market (>$2 billion)

- **Recombinant alternative to porcine pancreatic enzyme replacement therapy (PERT)**

- **A safer and more convenient therapy with a reduced daily pill burden**

- **Pursuing parallel monotherapy and combination therapy clinical pathways**

- **New enteric microgranule formulation developed**
- **Phase 2 bridging study trial initiated – January 2023**
- **Topline data anticipated in July 2023**

First Wave BioPharma

NICLOSAMIDE
IBD Opportunity

www.firstwavebio.com

Significant Unmet Need in IBD

Between 1.6 million and 3.1 million[1] patients in the U.S are estimated to have IBD (Ulcerative Colitis and Crohn's Disease)

- Estimates of direct and indirect IBD healthcare costs range between $15 billion and $32 billion[3]
- A chronic condition with unexpected GI exacerbations which can be painful, inconvenient and embarrassing
- The 'real' price of IBD may be the reduced quality of life and ability to work and associated emotional burden and social stigma

[1] Crohns and Colitis Foundation 2022
[2] Kaplan, G. The global burden of IBD: from 2015 to 2025. *Nature Reviews Gastroenterology & Hepatology* Vol. 12, pp. 720–727 (2015)

Current Treatments Are Ineffective

Diagnosis

- Patient has mild to moderate ulcerative colitis

Treatment

- Treat patient with 5-ASA (oral, rectal, or both together) in the hope of inducing and maintaining remission

Result

- Remission fails to occur in patients all too often

  ~54% fail remission with oral 5-ASA[1]

  ~59% fail remission with rectal 5-ASA[2]

[1] Wang, Y. et al. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochrane Database of Systematic Reviews*. August 2020.; Feagan, B. and Macdonald, J. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochrane Database Syst Rev.* 2012 Oct 17;10:CD000543.
[2] Ham, M. and Moss, C. Mesalamine in the treatment and maintenance of remission of ulcerative colitis. Expert Rev Clin Pharmacol. 2012 Mar; 5(2): 113–123.

IBD Opportunity (U.S.)

UC Prevalence: ~830K people (700K mild-moderate)

UC Market Size: $5 Billion ($4.6B mild-moderate)

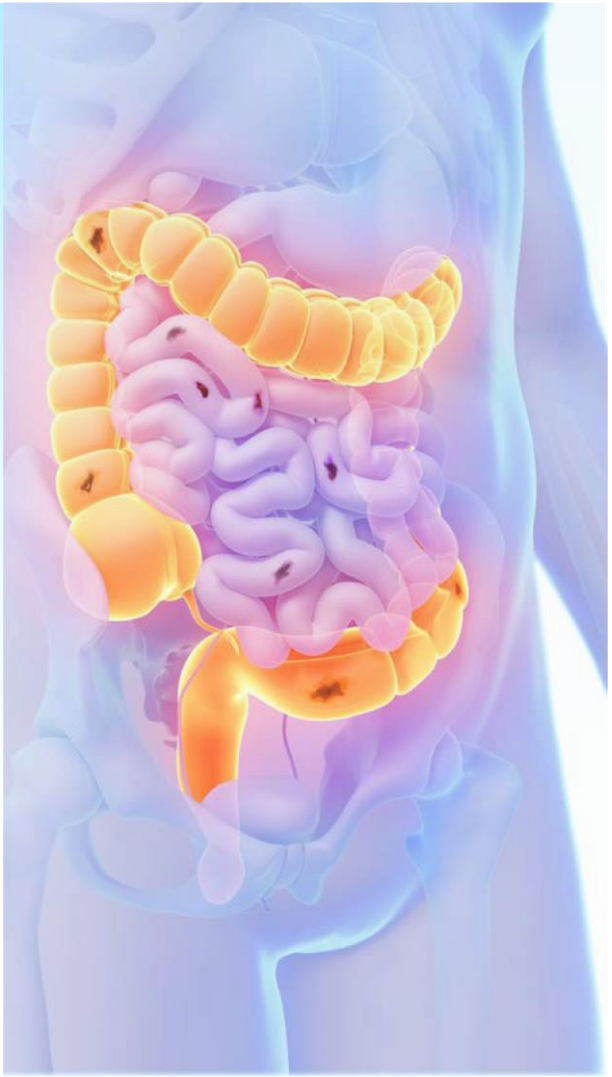
CD Prevalence: ~660K people (500K mild-moderate)

CD Market Size: $7.4 Billion ($4.3B mild-moderate)

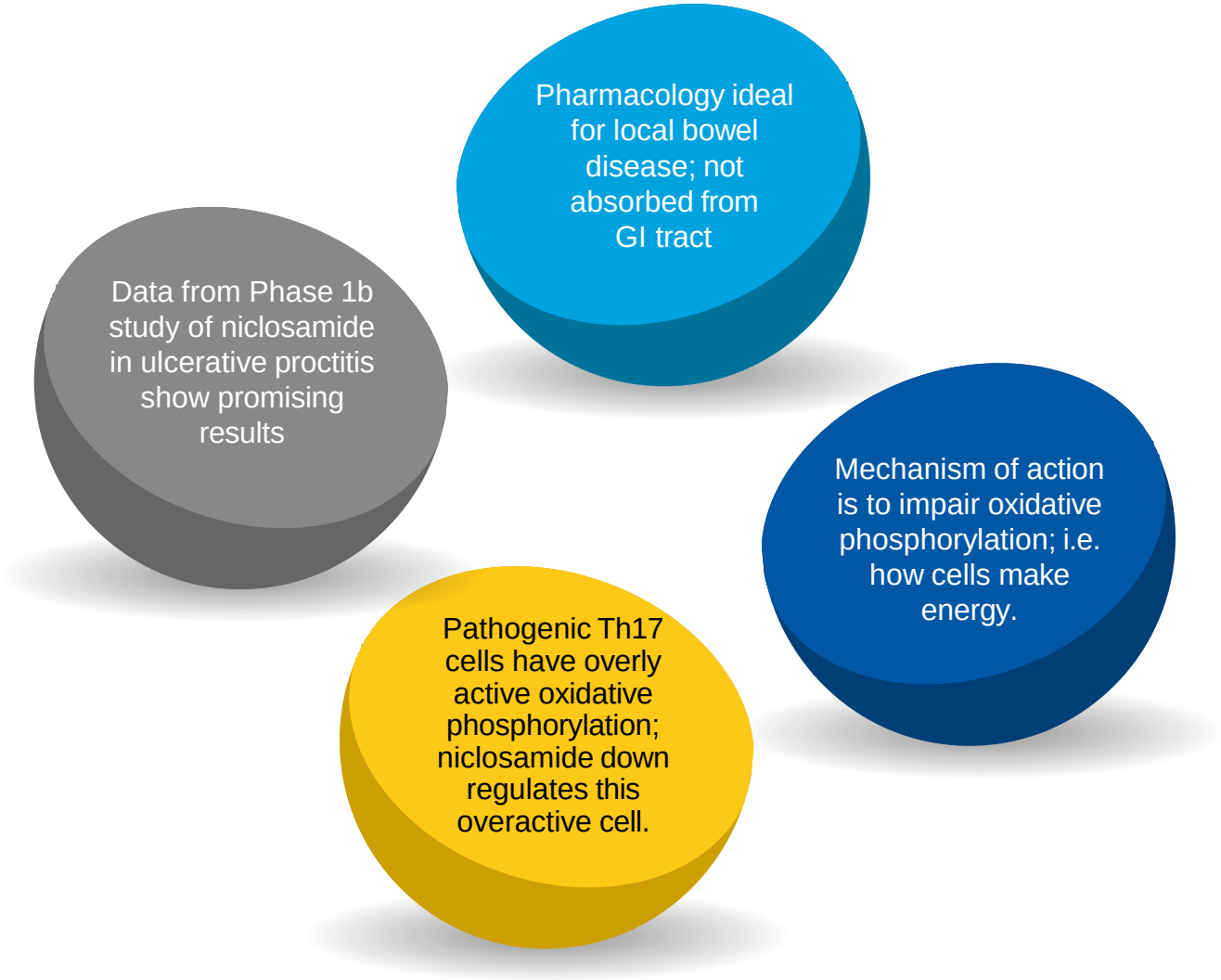
Sources: GlobalData Ulcerative Colitis Global Drug Forecast and Market Analysis to 2026: US Adults. 2018; GlobalData Crohn's Disease Global Drug Forecast and Market Analysis to 2029: US. 2020

History and Safety Profile of Niclosamide

- **FDA approved (1982) small molecule anthelmintic drug used for intestinal tapeworm infections**
- **Clean safety history**
- **Ideal profile for GI-targeted agent**
  - Low oral bio-availability with minimal systemic exposure
  - Niclosamide inhibits pro-inflammatory pathways
  - Non-steroidal anti-inflammatory option
  - Opportunities for combinations with standard of care for multiple indications without systemic immunosuppression



Role for Niclosamide in IBD
A Unique Mechanism of Action



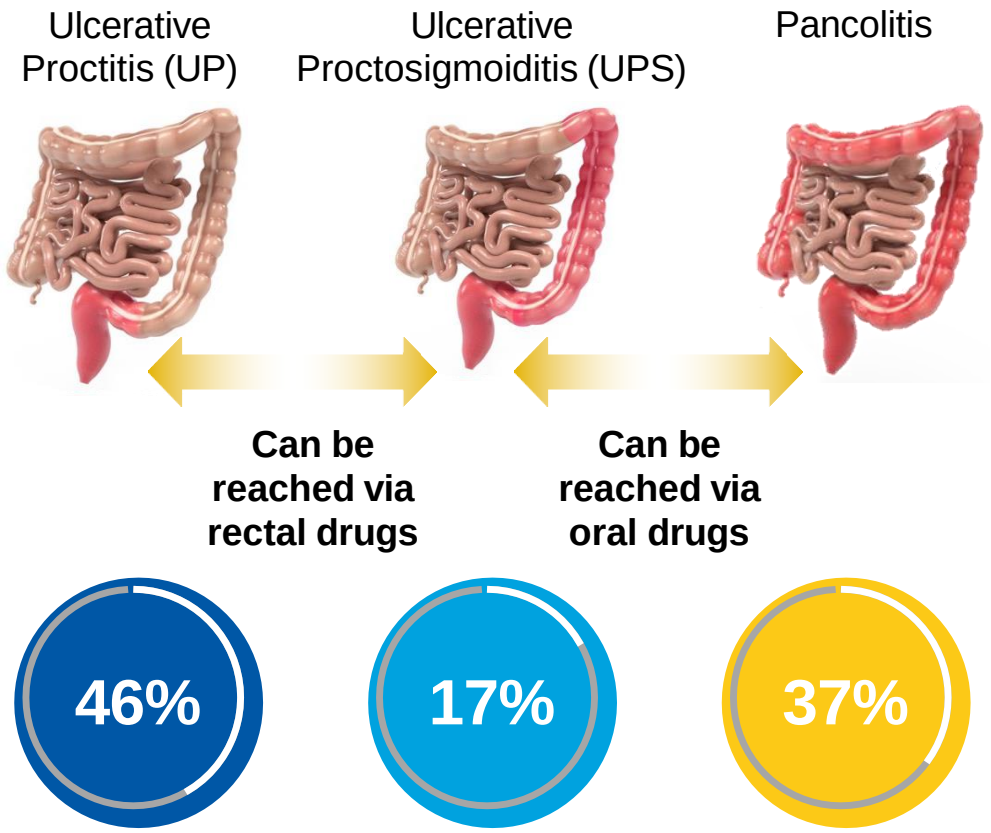
Rationale for Conducting Initial Proof-of-Concept in UC

Significant unmet medical need, particularly in patients that fail 5-ASA

UC is easily monitored by serial endoscopy, which provides objective endpoints

>60% of patients have disease that can be treated rectally, which provides rapid path to evaluate POC with rectal delivery

Data will inform rectal and oral development program in UC



Distribution of disease location across UC patients

Developmental Pathway: Oral Micronized Niclosamide Tablets to Treat UC and CD

Focused on Phase 2 Adrulipase Bridging Study in 1H 2023

Program	Preclinical	Phase 1	Phase 2	Phase 3	Next milestone
Adrulipase					
Monotherapy (FW-EPI)			**Exocrine pancreatic insufficiency in cystic fibrosis – enteric microgranule formulation** Phase 2 Bridging Study		Topline Data 2H'23
Monotherapy (FW-EPI)			**Exocrine pancreatic insufficiency in cystic fibrosis** Phase 2b Topline data: Q1'21		
Combination (FW-EPI+ PERT)			**Severe exocrine pancreatic insufficiency in cystic fibrosis** Phase 2 Topline data: Q3'21		
Niclosamide					
FW-UP			**IBD: Ulcerative colitis-proctitis** Phase 2 Initiation: Q3'21		Phase 2 Topline data: 2H'22
FW-ICI-AC			**Immune checkpoint inhibitor colitis** Phase 2 IND clearance: Q4'21		Phase 2a Initiation*

* Anticipated