First Wave BioPharma

September 2022

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
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

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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

- **~30,000 patients U.S., ~100,000 worldwide**
- Treatment begins for patients in first six months of life

Chronic Pancreatitis

Heterogeneous disease

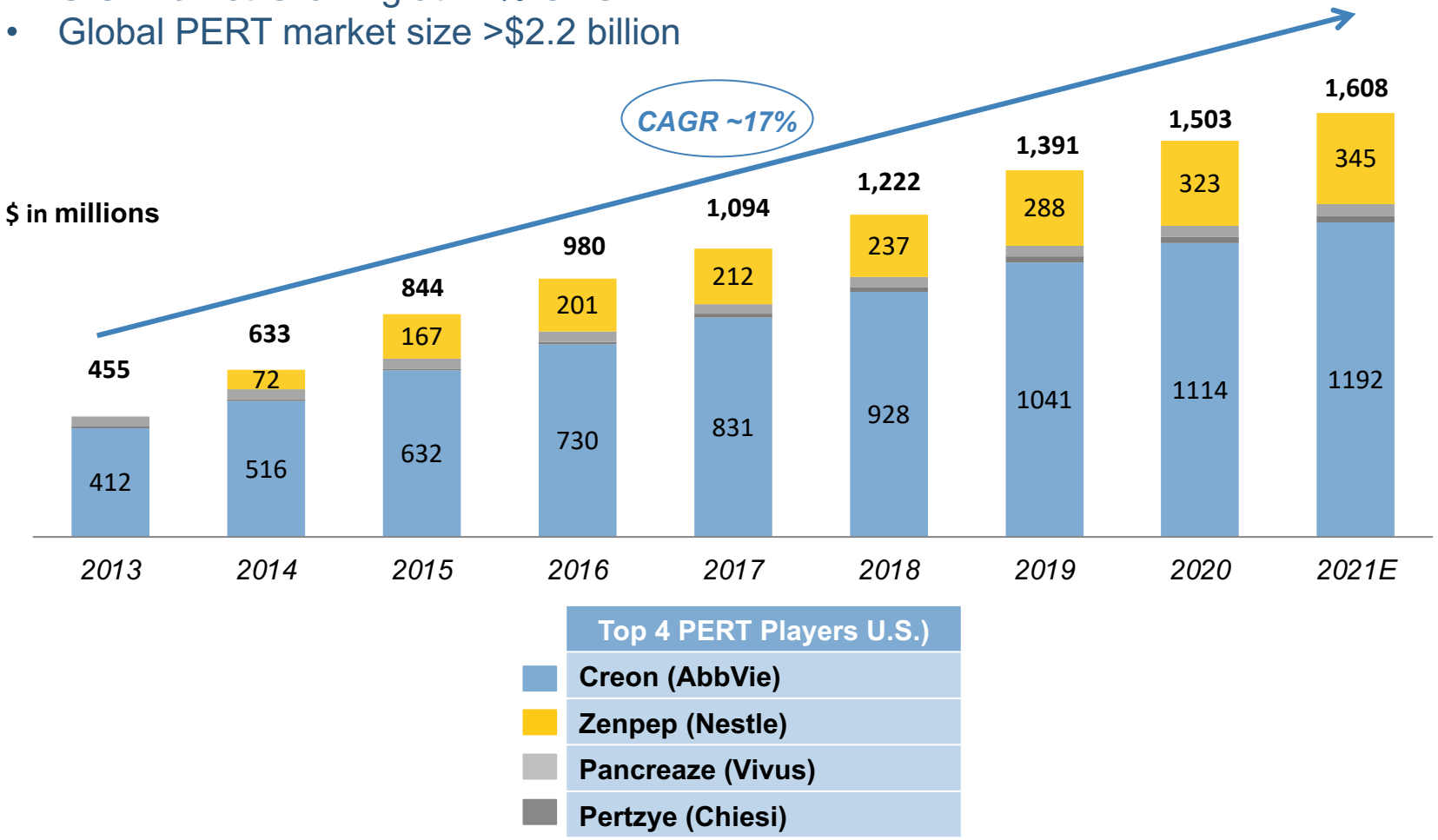
- **~90,000 patients U.S., ~450K-600K worldwide**
- Alcoholism
- Pancreatic cancer
- Pancreatic surgery

Sources: The CorStar Group 2019. Cystic Fibrosis Foundation 2020. National Pancreas Foundation 2020..

Large Established U.S. Market Of ~$1.6 Billion(1)

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

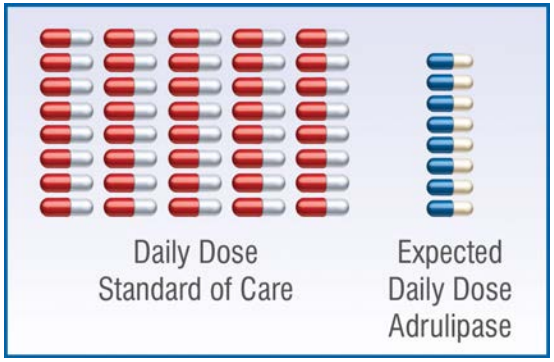
- U.S. Market Growing at 17% CAGR
- Global PERT market size >$2.2 billion

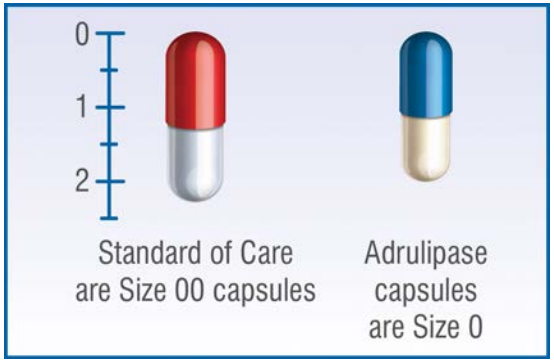


Sources: Global Market Size: Symphony Health 2019. The CorStar Group (2019). U.S. Market Size: Creon 2013-2020 AbbVie 10-K's, 2021 Mgmt. Estimate; Zenpep, Allergan 2014-2020 10-Ks, 2021 Mgmt. Estimate; Vivus and Pertzye.

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 and cannot dose up	▪ **Safe and well tolerated to date** ▪ No fibrosing colonopathy
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: FW-EPI Clinical Program
Recombinant lipase for treating Exocrine Pancreatic Insufficiency

- Targeting patients with **Cystic Fibrosis (CF)** and **Chronic Pancreatitis (CP)**
- ~ 30,000 CF patients and ~ 90,000 CP patients in the U.S.
- Addressing established global market (>$2 billion)(1)

Recombinant alternative to porcine pancreatic enzyme replacement therapy (PERT)	▪ Clear unmet medical need ▪ Demonstrated safety and efficacy profile in two Phase 2 clinical trials in two indications
Pursuing parallel monotherapy and combination therapy clinical pathways	▪ Topline Phase 2b CF monotherapy data announced in Q1 2021 ▪ Topline Interim Phase 2 CF combination (Adrulipase + PERT) therapy data announced in Q3 2021

- **New enteric granule formulation being developed**
- **Phase 2 trial anticipated in 2H 2022**

Sources: The CorStar Group 2019. Symphony Health 2019. Cystic Fibrosis Foundation 2020. National Pancreas Foundation 2020.

Lessons Learned From the Adrulipase Program and Next Steps

Four Phase 2 Studies to Date: • Cystic Fibrosis & Chronic Pancreatitis • Monotherapy & Combination Therapy 1	Product has evidence of lipase activity 2	Product shows dose-response in chronic pancreatitis 3	Combination therapy with PERT shows clinically meaningful improvement for less controlled patients with Severe EPI in cystic fibrosis 4
Safety is excellent at all doses studied 5	Despite lack of protease, CNAs are consistently >80% 6	Powder formulation in immediate release or enteric capsules was not sufficient to obtain consistent CFAs >80% 7	Formulation with good gastric dispersion plus gastric acid protection logical next step 8

Next Steps	Enteric Microgranule Formulation Development	Phase 2 FW-EPI Monotherapy Trial 2H 2022

Current Commercial Grade Adrulipase Projections

Significantly Lower Pill Burden and Commercially Attractive COGS Due to Manufacturing Optimization and Reformulation

		Option2 / CP				
	Process Step / Description	2020 GMP Batch	CURRENT		TARGET	
			50m3	100m3	50m3	100m3
Drug Substance	Fermentation Lipase Conc. (g/L)	# -	# +++		# ++++	
	DS Process Yield	%+	%+		% ++	
	Cost of Lipase ($/kg)	$ --	$ ++	$ +++	$ ++++	$ +++++
Drug Product	Lipase / 00 Capsule (mg)	# +	# ++++	# ++++	# ++++	# ++++
	Cost / Capsule	$ ++	$ +	$ ++	$ +++	$ ++++
	Patient Capsules / Day (Middle Dose)	16	5-8	5-8	5-8	5-8
	Patient Cost / Month (Middle Dose)	$ -	$ +	$ ++	$ +++	$ ++++
	Reduction in Patient Cost / Month From 2020 GMP Batch Projections		**70%**	**79%**	**82%**	**87%**
		Adapted to 50m3 scale				

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NICLOSAMIDE
IBD Opportunity

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)

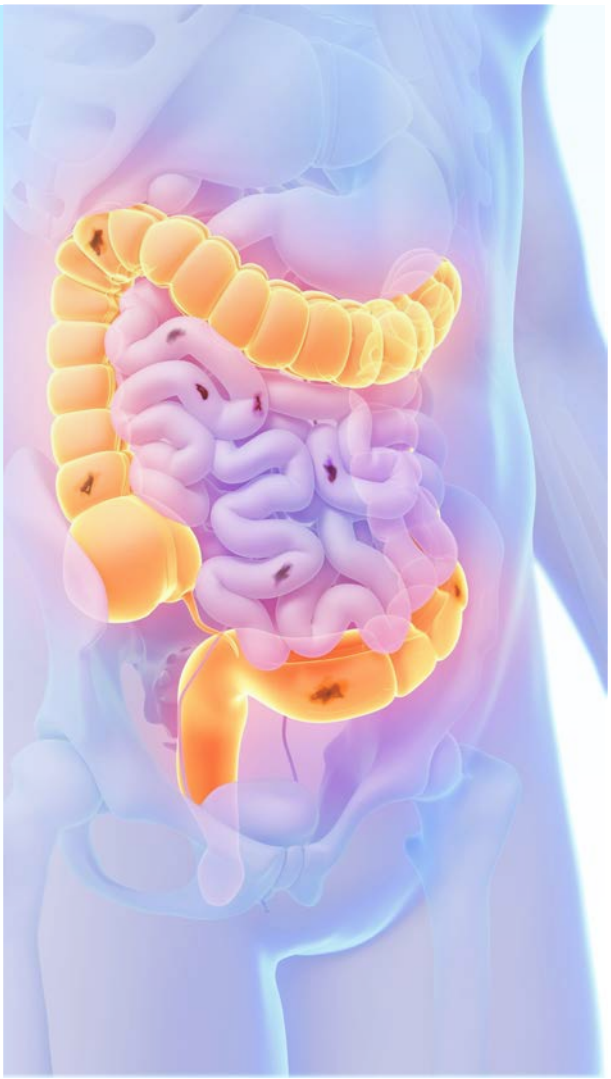
CD Prevalence: ~660K people (500K mild-moderate)

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

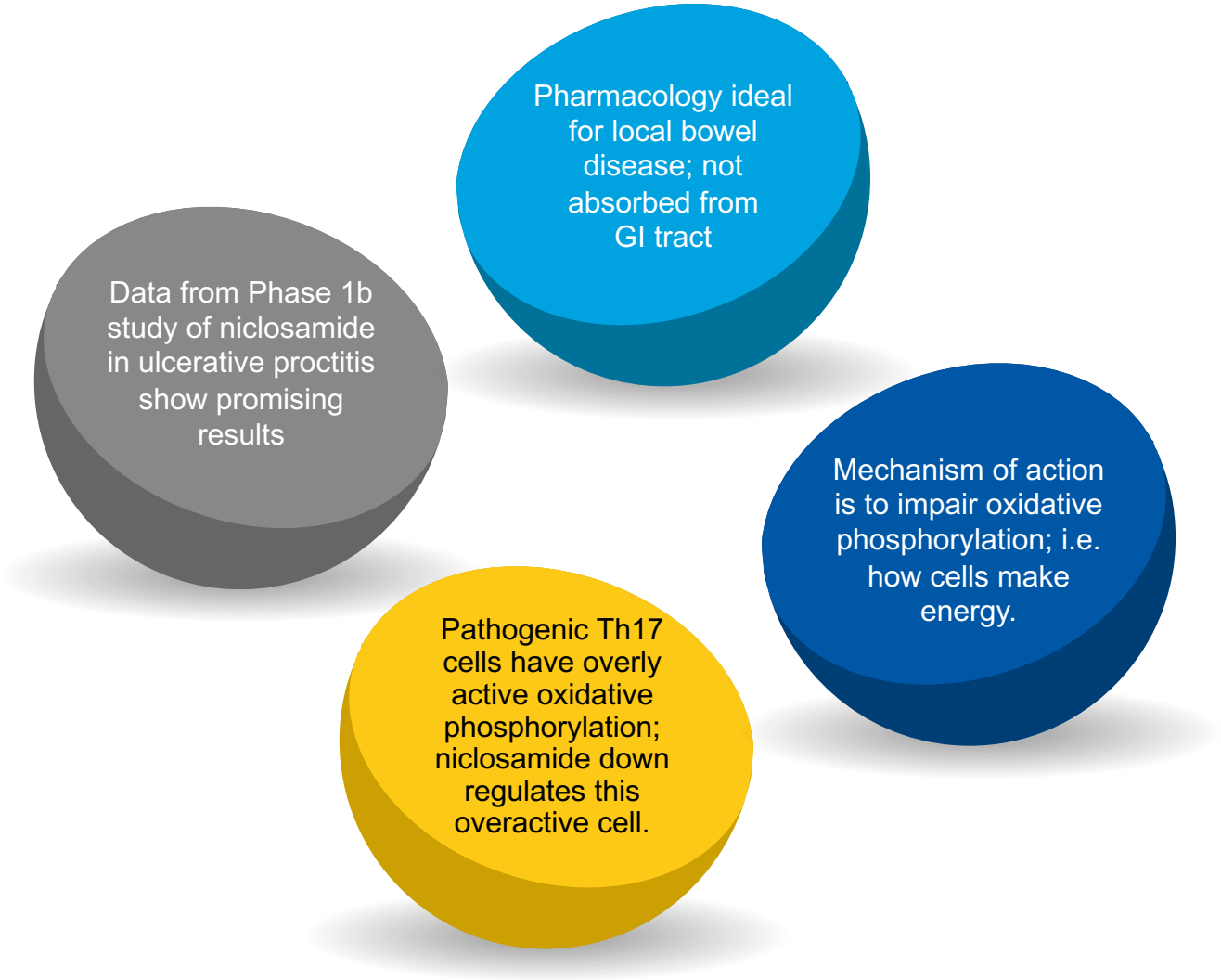
Sources: GlobalData Ulcerative Colitis Global Drug Forecast and Market Analysis to 2026: US Adults. 2018; GlobalData Crohn's Disease Global Drug Forecast and Market Analysis to 2029: US. 2020

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



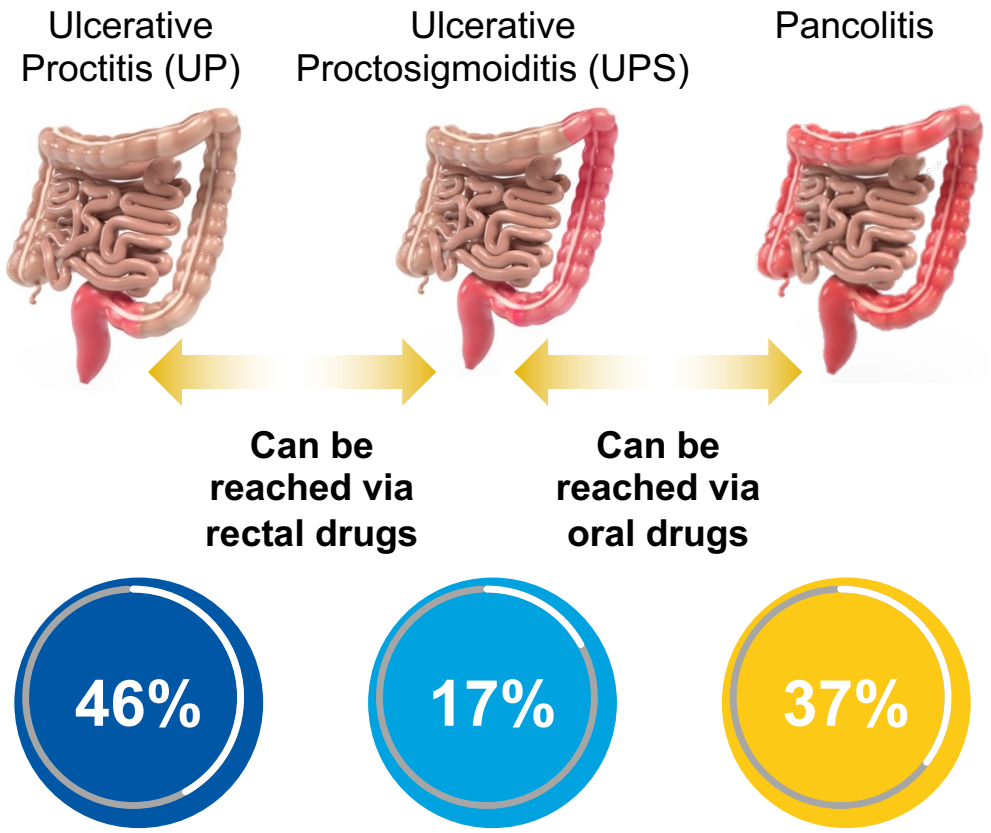
Rationale for Conducting Initial Proof-of-Concept in UC

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

Major Inflection Points with Three Clinical Stage Programs in 2022

Program	Preclinical	Phase 1	Phase 2	Phase 3	Next milestone
Adrulipase					
Monotherapy (FW-EPI)	**Exocrine pancreatic insufficiency in cystic fibrosis** Phase 2b Topline data: Q1'21				Phase 2 Enteric formulation trial initiation: 2H'22*; anticipated completion 1H'23
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