



January 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

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



James Pennington, MD
Chief Medical Officer



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

- 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



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

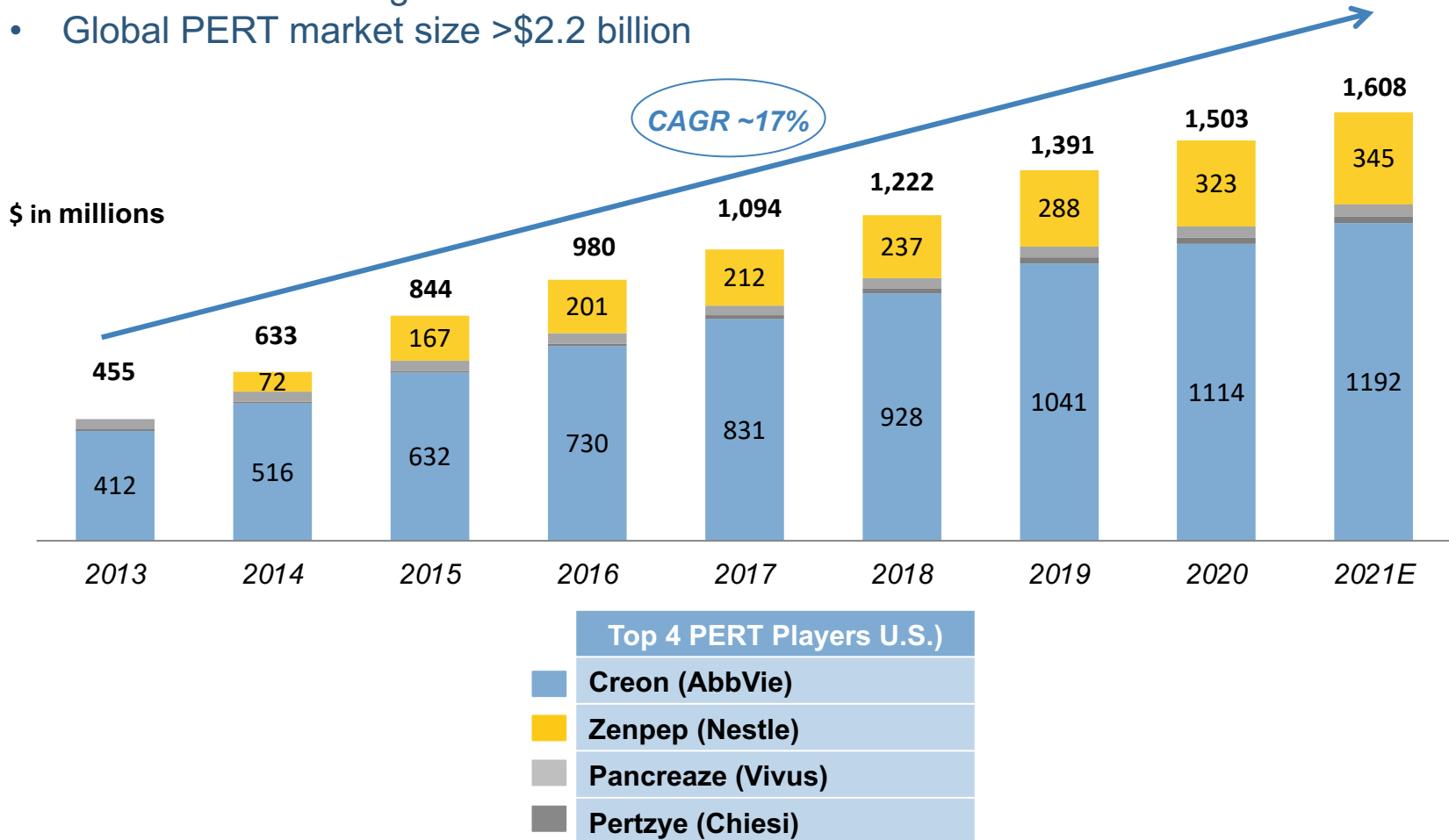
- ~90,000 patients U.S.,
~450K-600K worldwide
- Alcoholism
- Pancreatic cancer
- Pancreatic surgery

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

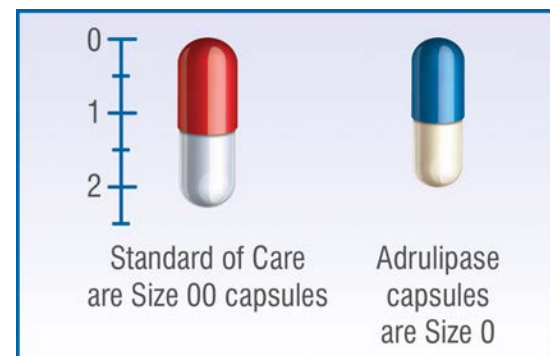
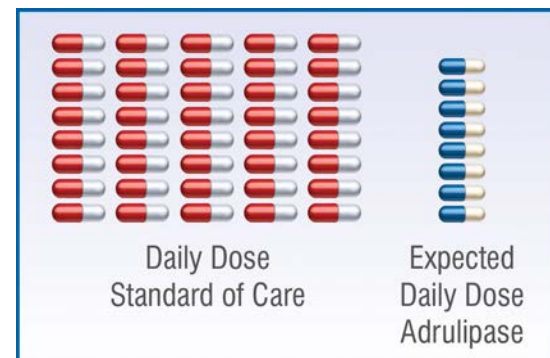
- U.S. Market Growing at 17% CAGR
- Global PERT market size >\$2.2 billion



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 Pertzeye.

Adrulipase: Fulfilling an Unmet Medical Need

	PERT	ADRULIPASE
Drug Substance	<ul style="list-style-type: none"> ▪ Porcine-derived pancreatic enzyme replacement therapy (PERT) 	<ul style="list-style-type: none"> ▪ Recombinant yeast (<i>Yarrowia lipolytica</i>) lipase-derived replacement therapy
Safety	<ul style="list-style-type: none"> ▪ Adverse event: fibrosing colonopathy at high doses ▪ FDA black box warning ▪ ~30% of CF patients are not well controlled on PERT 	<ul style="list-style-type: none"> ▪ Safe and well tolerated to date ▪ No fibrosing colonopathy
Pill Burden	<ul style="list-style-type: none"> ▪ 25-40 pills per day (CF) 	<ul style="list-style-type: none"> ▪ 5-8 pills per day (CF)
Sourcing & Supply	<ul style="list-style-type: none"> ▪ Subject to pig herd management ▪ Risk of transmission of animal pathogens ▪ Manufacturing + supply chain inconsistency 	<ul style="list-style-type: none"> ▪ 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 (Aadrulipase + PERT) therapy data announced in Q3 2021

- New enteric granule formulation developed
- Phase 2 trial initiation anticipated in 1H 2023

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

Lessons Learned From the Aadrulipase Program and Next Steps

<p>Four Phase 2 Studies to Date:</p> <ul style="list-style-type: none"> • Cystic Fibrosis & Chronic Pancreatitis • Monotherapy & Combination Therapy 	<p>Product has evidence of lipase activity</p>	<p>Product shows dose-response in chronic pancreatitis</p>	<p>Combination therapy with PERT shows clinically meaningful improvement for less controlled patients with Severe EPI in cystic fibrosis</p>
<p>Safety is excellent at all doses studied</p>	<p>Despite lack of protease, CNAs are consistently >80%</p>	<p>Powder formulation in immediate release or enteric capsules was not sufficient to obtain consistent CFAs >80%</p>	<p>Formulation with good gastric dispersion plus gastric acid protection logical next step</p>

<p>Next Steps</p>	<p>Enteric Microgranule Formulation Development</p>	<p>Phase 2 FW-EPI Monotherapy Trial 1H 2023</p>
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Current Commercial Grade Adrulipase Projections

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

		Option2 / CP	CURRENT		TARGET	
Process Step / Description		2020 GMP Batch	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				



NICLOSAMIDE IBD Opportunity

Significant Unmet Need in IBD

Between 1.6 million and 3.1 million¹ 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 billion³
- 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-ASA¹
 - ~59% fail remission with rectal 5-ASA²

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

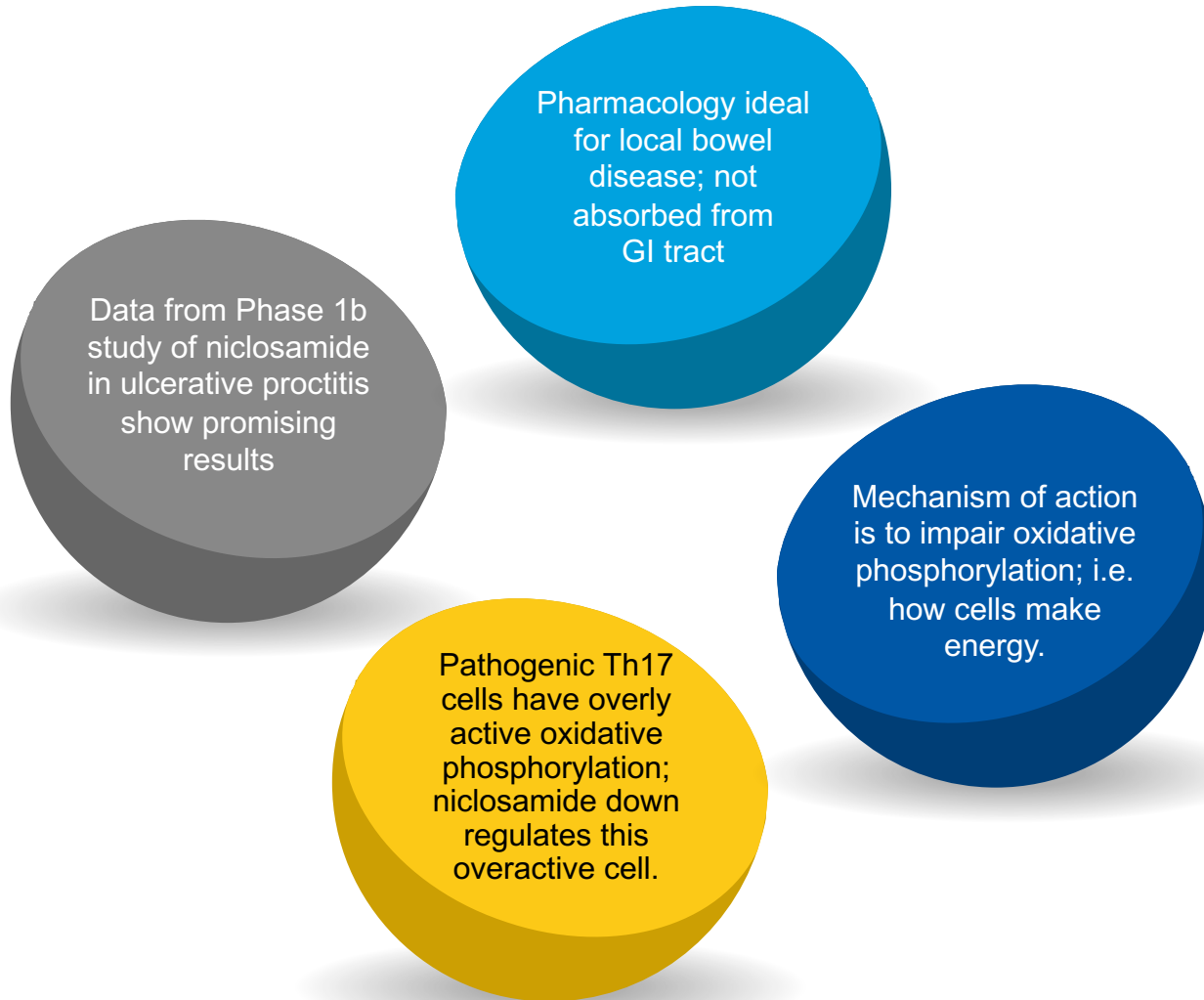
History and Safety Profile of Niclosamide

- **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



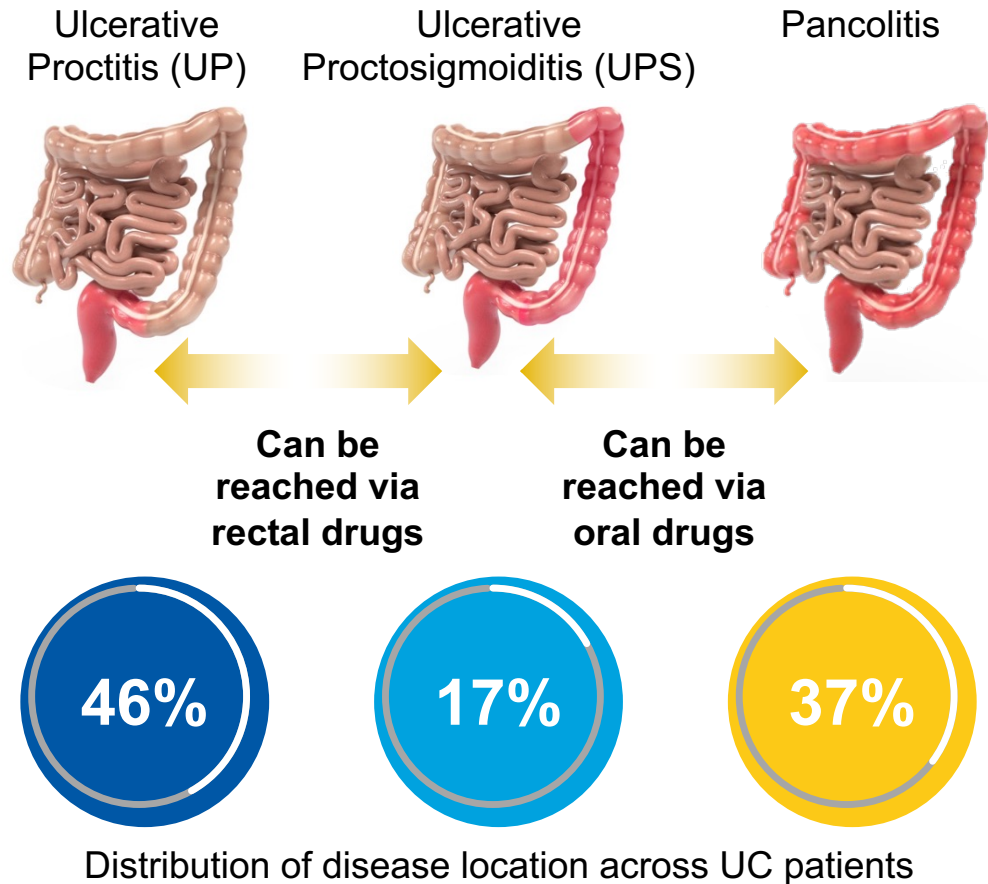
Rationale for Conducting Initial Proof-of-Concept in UC

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



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

Focused on Phase 2b 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 Phase 2b Topline data: Q1'21				Phase 2 Enteric formulation trial initiation: Q1'23*; 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