



August 2022

# CORPORATE PRESENTATION

(NASDAQ:FWBI)

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

# Company Disclaimer

*Certain statements in this presentation constitute “forward-looking statements” within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. Any statements that refer to expectations or other characterizations of future events, circumstances or results are forward-looking statements. Such forward-looking statements include projections. Such projections were not prepared in accordance with public guidelines of the American Institute of Certified Public Accountants regarding projections and forecasts, nor have such projections been audited, examined or otherwise reviewed by independent auditors of the company. Such forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of the company and its clinical trials to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements.*

*The views expressed are those of management and are based on currently available information. Estimates and projections contained herein have been prepared by management and involve significant elements of subjective judgment and analysis and are based on certain assumptions. No representation nor warranty, expressed or implied, is made as to the accuracy or completeness of the information contained in this document, and nothing contained herein is, or shall be relied upon, as a promise or representation, whether as to the past or the future. The projections are not intended to follow generally accepted accounting principles. Neither our accountants nor our legal counsel have compiled, audited, prepared, or contributed to the projections or the underlying assumptions. None of these parties express an opinion with respect to the projections.*

*You are cautioned not to place undue reliance on these forward-looking statements. Except for ongoing obligations of the company to disclose material information under the federal securities laws, the company does not undertake any obligation to release any revisions to any forward-looking statements, to report events or to report the occurrence of unanticipated events.*

## 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

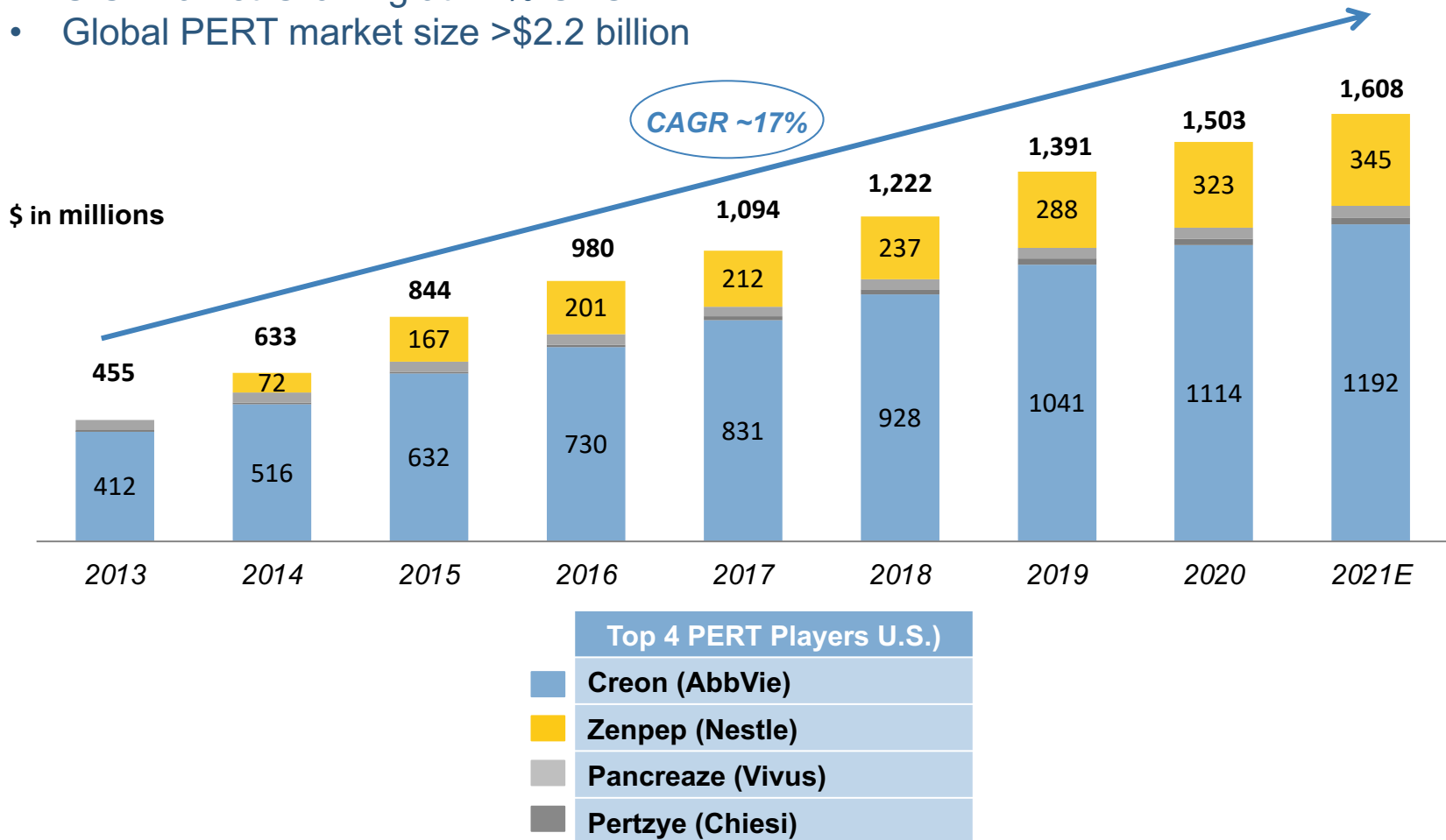
- ~90,000 patients U.S.,  
~450K-600K worldwide
- Alcoholism
- Pancreatic cancer
- Pancreatic surgery

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

## Large Established U.S. Market Of ~\$1.6 Billion<sup>(1)</sup>

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

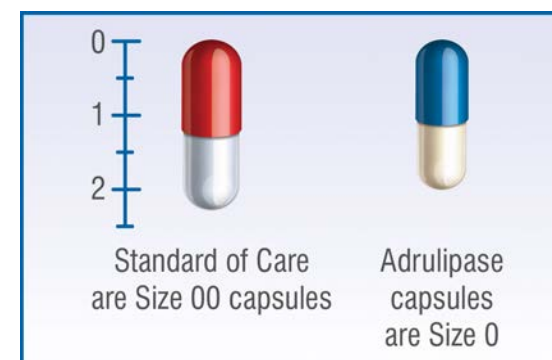
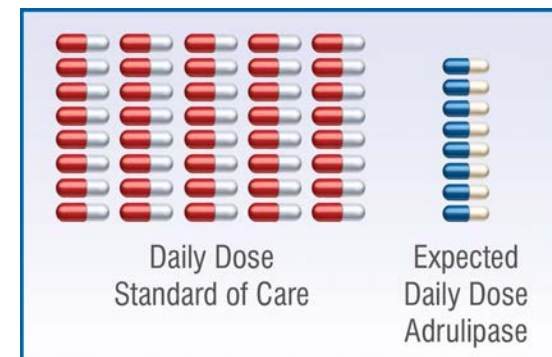
- U.S. Market Growing at 17% CAGR
- Global PERT market size >\$2.2 billion



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"> <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> </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.



# 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)<sup>(1)</sup>

### 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 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 Aadrulipase Program and Next Steps

<p>Four Phase 2 Studies to Date:</p> <ul style="list-style-type: none"> <li>• Cystic Fibrosis &amp; Chronic Pancreatitis</li> <li>• Monotherapy &amp; Combination Therapy</li> </ul>	<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 &gt;80%</p>	<p>Powder formulation in immediate release or enteric capsules was not sufficient to obtain consistent CFAs &gt;80%</p>	<p>Formulation with good gastric dispersion plus gastric acid protection logical next step</p>

<p><b>Next Steps</b></p>	<p>Enteric Microgranule Formulation Development</p>	<p>Phase 2 FW-EPI Monotherapy Trial 2H 2022</p>
--------------------------	---	---

## 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)	\$ -	\$ +	\$ ++	\$ +++	\$ +++++
<b>Reduction in Patient Cost / Month From 2020 GMP Batch Projections</b>			<b>70%</b>	<b>79%</b>	<b>82%</b>	<b>87%</b>
		Adapted to 50m3 scale				



# NICLOSAMIDE IBD Opportunity

## Significant Unmet Need in IBD

Between 1.6 million and 3.1 million<sup>1</sup> 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<sup>3</sup>
- 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

<sup>1</sup> Crohns and Colitis Foundation 2022

<sup>2</sup> 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<sup>1</sup>
  - ~59% fail remission with rectal 5-ASA<sup>2</sup>

<sup>1</sup> 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.

<sup>2</sup> 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

Data from Phase 1b study of niclosamide in ulcerative proctitis show promising results

Pharmacology ideal for local bowel disease; not absorbed from GI tract

Pathogenic Th17 cells have overly active oxidative phosphorylation; niclosamide down regulates this overactive cell.

Mechanism of action is to impair oxidative phosphorylation; i.e. how cells make energy.

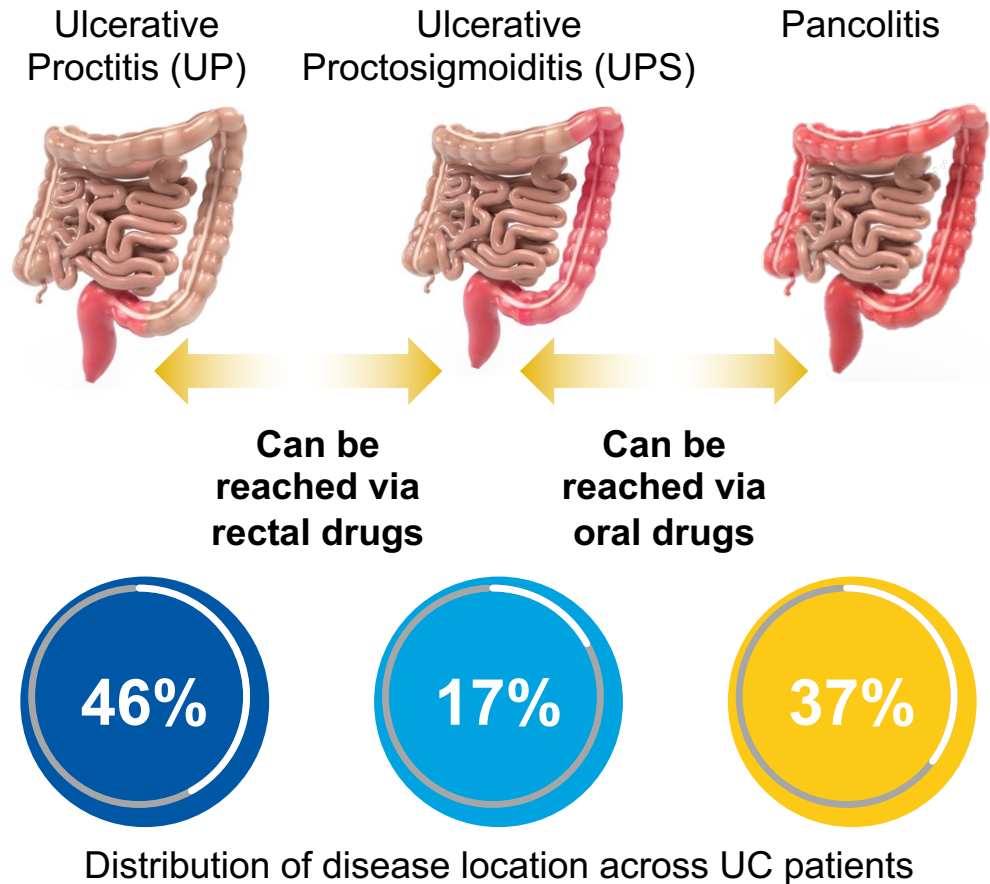
# Rationale for Conducting Initial Proof-of-Concept in UC

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

# Major Inflection Points with Three Clinical Stage Programs in 2022

Program	Preclinical	Phase 1	Phase 2	Phase 3	Next milestone
<b>Adrulipase</b>					
<b>Monotherapy (FW-EPI)</b>	<b>Exocrine pancreatic insufficiency in cystic fibrosis</b> Phase 2b Topline data: Q1'21				Phase 2 Enteric formulation trial initiation: 2H'22*; anticipated completion 1H'23
<b>Combination (FW-EPI+ PERT)</b>	<b>Severe exocrine pancreatic insufficiency in cystic fibrosis</b> Phase 2 Topline data: Q3'21				
<b>Niclosamide</b>					
<b>FW-UP</b>	<b>IBD: Ulcerative colitis-proctitis</b> Phase 2 Initiation: Q3'21				Phase 2 Topline data: 2H'22*
<b>FW-ICI-AC</b>	<b>Immune checkpoint inhibitor colitis</b> Phase 2 IND clearance: Q4'21				Phase 2a Initiation*

\* Anticipated