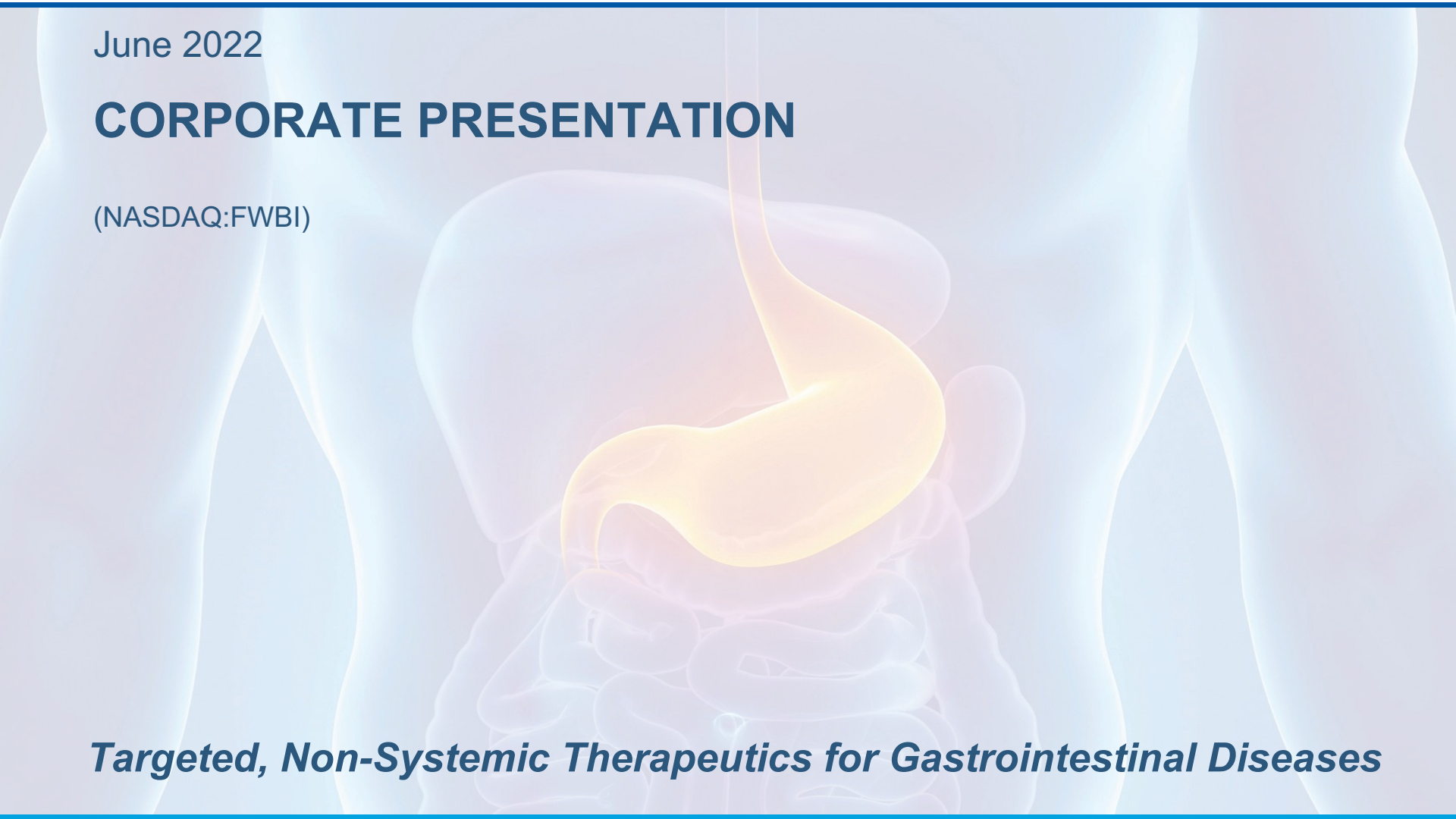
First Wave BioPharma

June 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 lipase biologic for the treatment of Exocrine Pancreatic Insufficiency (EPI)**<br>• EPI in Cystic Fibrosis (CF); new enteric formulation |
| **NICLOSAMIDE** | **Re-purposed small molecule drug with potent anti-inflammatory properties, proprietary micronized formulation**<br>• IBD: Ulcerative Colitis-Ulcerative Proctitis<br>• 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.**
- Treatment begins for patients in first six months of life

### Chronic Pancreatitis

**Heterogeneous disease**

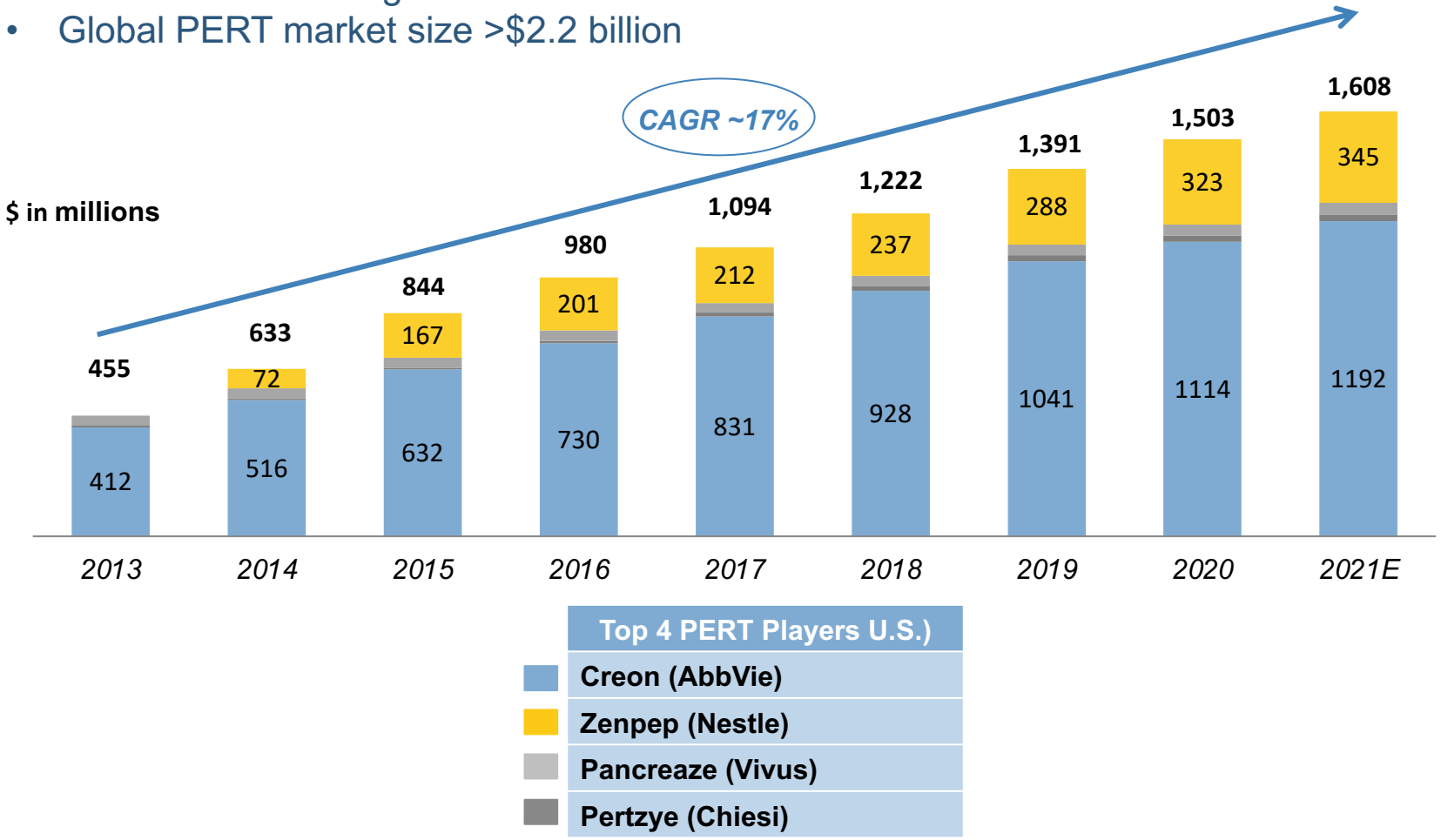
- **~90,000 patients U.S.**
- Alcoholism
- Pancreatic cancer
- Pancreatic surgery

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

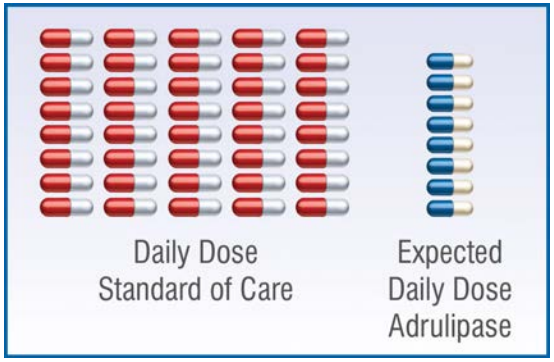


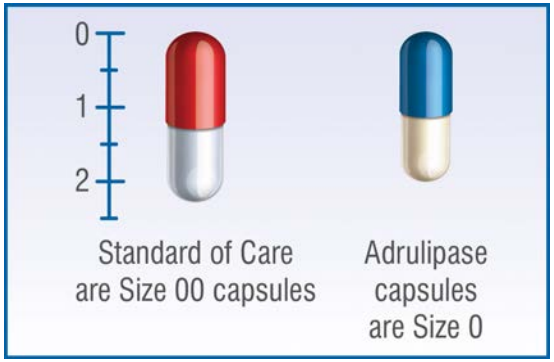

Sources: Global Market Size: Symphony Health 2019. The CorStar Group (2019). U.S. Market Size: Creon 2013-2020 AbbVie 10-K's, 2021 Mgmt. Estimate; Zenpep, Allergan 2014-2020 10-Ks, 2021 Mgmt. Estimate; Vivus and Pertzye.

# 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**<br>▪ FDA black box warning<br>▪ ~30% of CF patients are not well controlled on PERT and cannot dose up | ▪ **Safe and well tolerated to date**<br>▪ No fibrosing colonopathy |
| **Pill Burden** | ▪ **25-40 pills per day (CF)** | ▪ **5-8 pills per day (CF)** |
| **Sourcing & Supply** | ▪ Subject to pig herd management<br>▪ ***Risk of transmission of animal pathogens***<br>▪ Manufacturing + supply chain inconsistency | ▪ GRAS (Generally Regarded as Safe)<br>▪ ***No risk of animal pathogens***<br>▪ 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<br>▪ 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<br>▪ 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:<br>• Cystic Fibrosis & Chronic Pancreatitis<br>• Monotherapy & Combination Therapy<br>1 | Product has evidence of lipase activity<br>2 | Product shows dose-response in chronic pancreatitis<br>3 | Combination therapy with PERT shows clinically meaningful improvement for less controlled patients with Severe EPI in cystic fibrosis<br>4 |
| Safety is excellent at all doses studied<br>5 | Despite lack of protease, CNAs are consistently >80%<br>6 | Powder formulation in immediate release or enteric capsules was not sufficient to obtain consistent CFAs >80%<br>7 | Formulation with good gastric dispersion plus gastric acid protection logical next step<br>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

| | Process Step / Description | Option2 / CP 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 | 5 | 5 | 5 |
| | Patient Cost / Month (Middle Dose) | $ - | $ + | $ ++ | $ +++ | $ ++++ |
| | **Reduction Patient Cost / Month** | | **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
  - ✓*~58% fail remission with oral 5-ASA**
  - ✓*~50% fail remission with rectal 5-ASA**

# IBD Opportunity (U.S.)

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

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

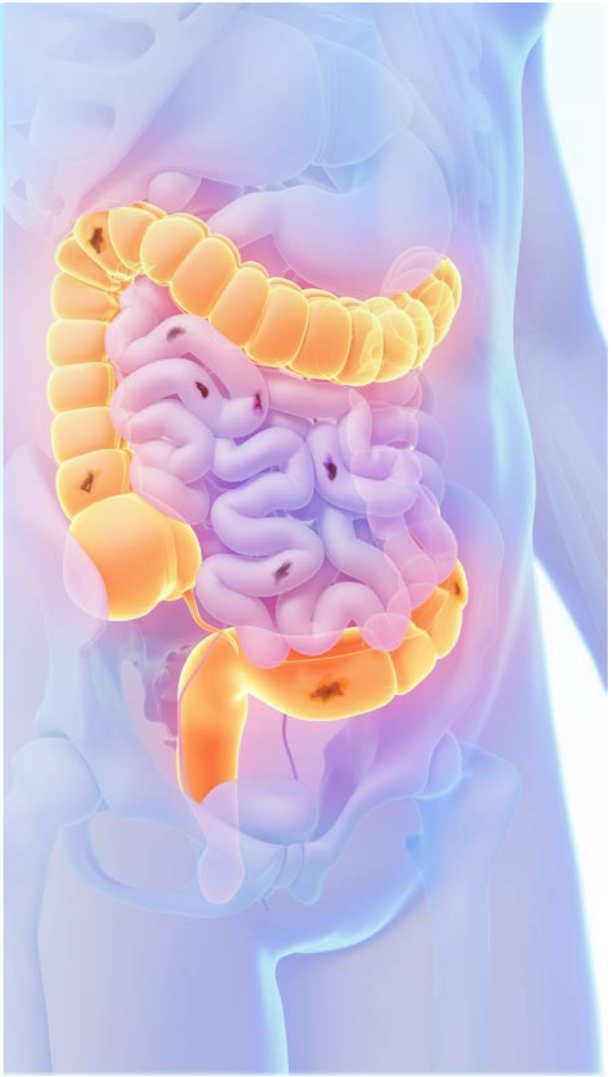
**CD Prevalence: ~660K people (500K mild-moderate)**

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

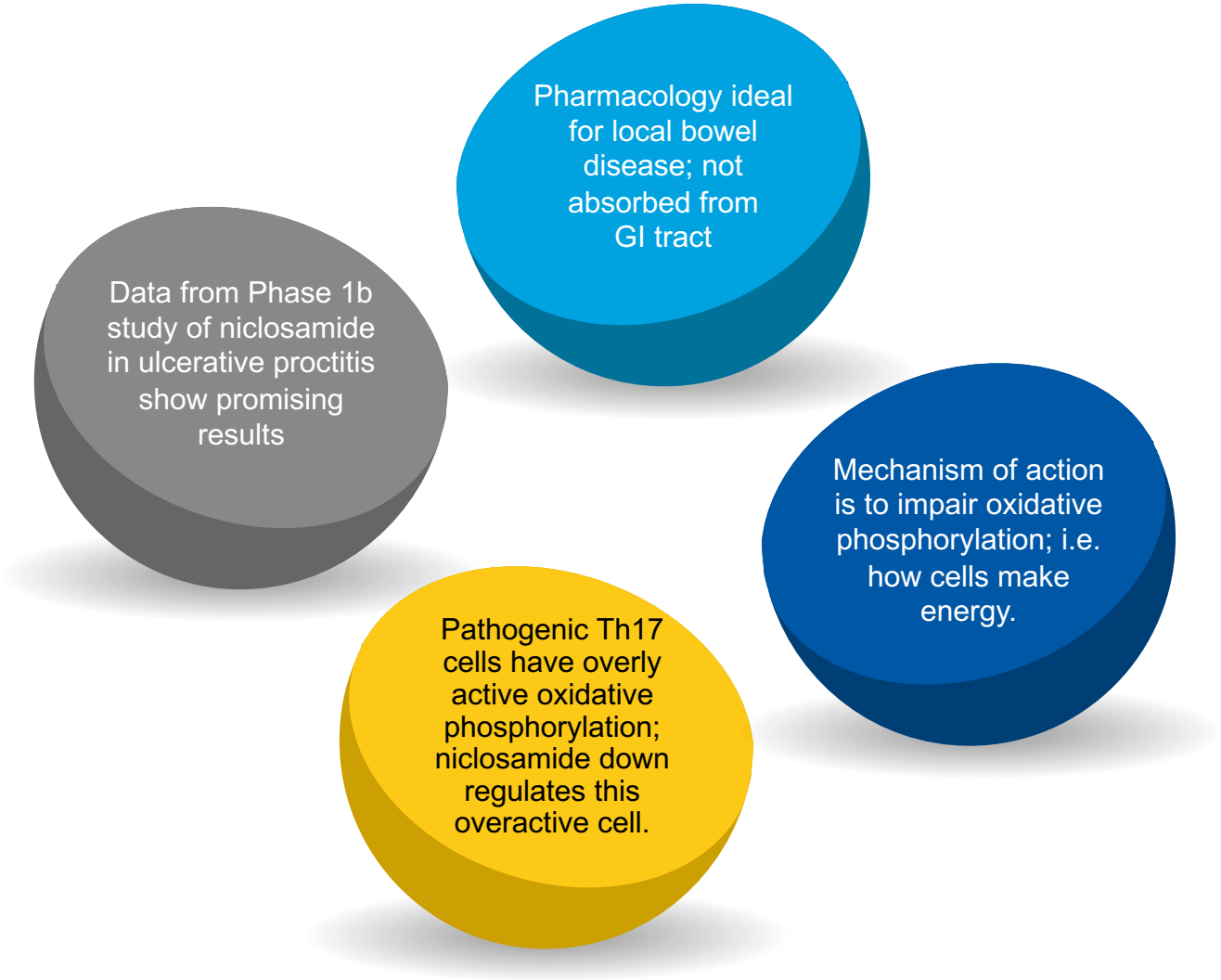
Sources: GlobalData Ulcerative Colitis Global Drug Forecast and Market Analysis to 2026: US Adults. 2018; GlobalData Crohn's Disease Global Drug Forecast and Market Analysis to 2029: US. 2020

# 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



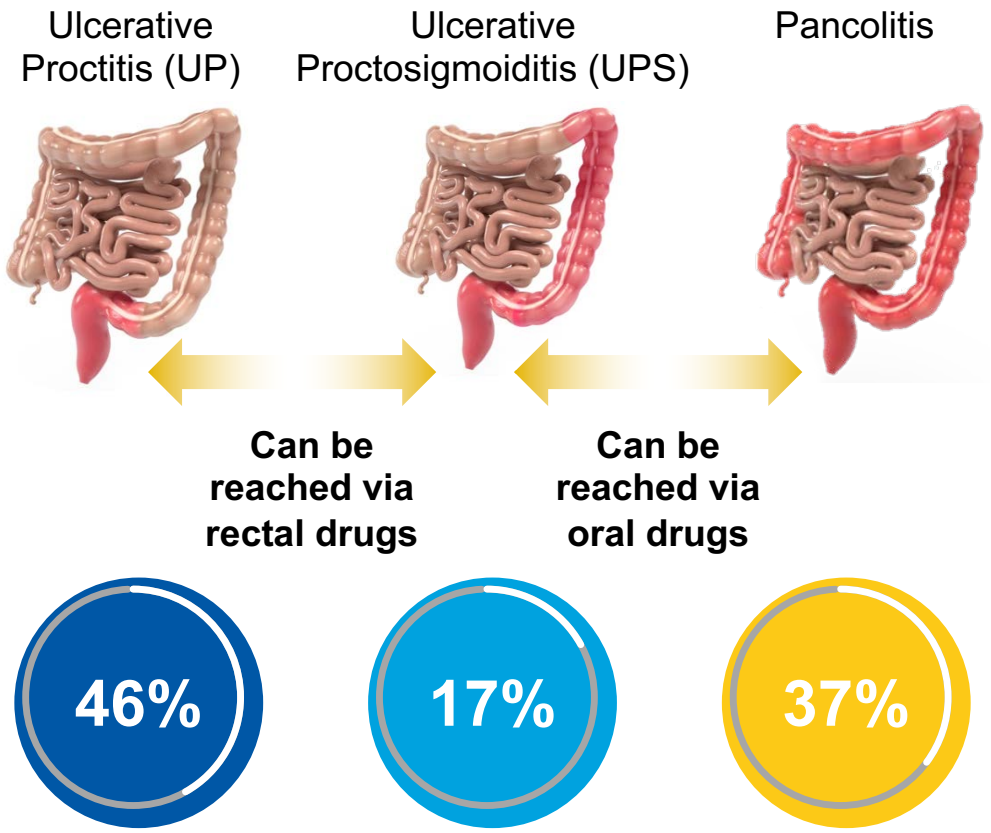
# Rationale for Conducting Initial Proof-of-Concept in UC

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* |
| **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