First Wave BioPharma

January 2022

CORPORATE PRESENTATION

(NASDAQ:FWBI)

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Overview

- **First Wave BioPharma** is a clinical stage biotechnology company currently focused on the development of targeted, non-systemic therapies for gastrointestinal (GI) diseases, with two assets and six clinical indications spanning inflammatory bowel diseases (IBD), COVID viral infections, oncology therapy induced colitis, and pancreatic digestive disorders.

Niclosamide:

- Re-purposed small molecule drug with potent anti-viral and anti-inflammatory properties, proprietary micronized formulation
  1. **COVID-19 GI infections (Phase 2 launched 1H 2021, enrollment completed Jan 2022)**
  2. **IBD: Ulcerative Colitis-Ulcerative Proctitis (Phase 2a launched in 2H 2021)**
  3. **Immune Checkpoint Inhibitor-Associated Colitis (Phase 2a IND clearance 2H 2021)**

Adrulipase:

- Recombinant lipase biologic for the treatment of Exocrine Pancreatic Insufficiency (EPI)
  4. **EPI in Cystic Fibrosis (CF); new enteric formulation (Phase 2b in 2H 2022)**

- Assets leverage the Company's core competencies and expertise in developing targeted, safe, non-systemic oral GI therapies
- 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

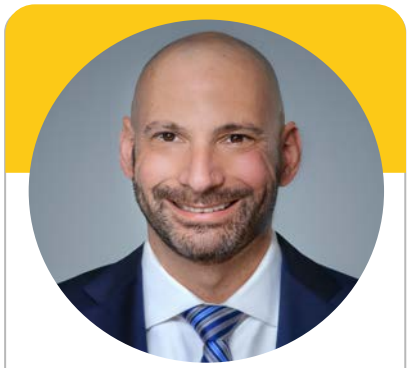
serono biotech & beyond
TOBIRA THERAPEUTICS
Lilly
GILEAD
Roche
Bristol-Myers Squibb

- 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

Bayer HealthCare Pharmaceuticals
COTHERIX
INTERMUNE
Anthera
HARVARD MEDICAL SCHOOL

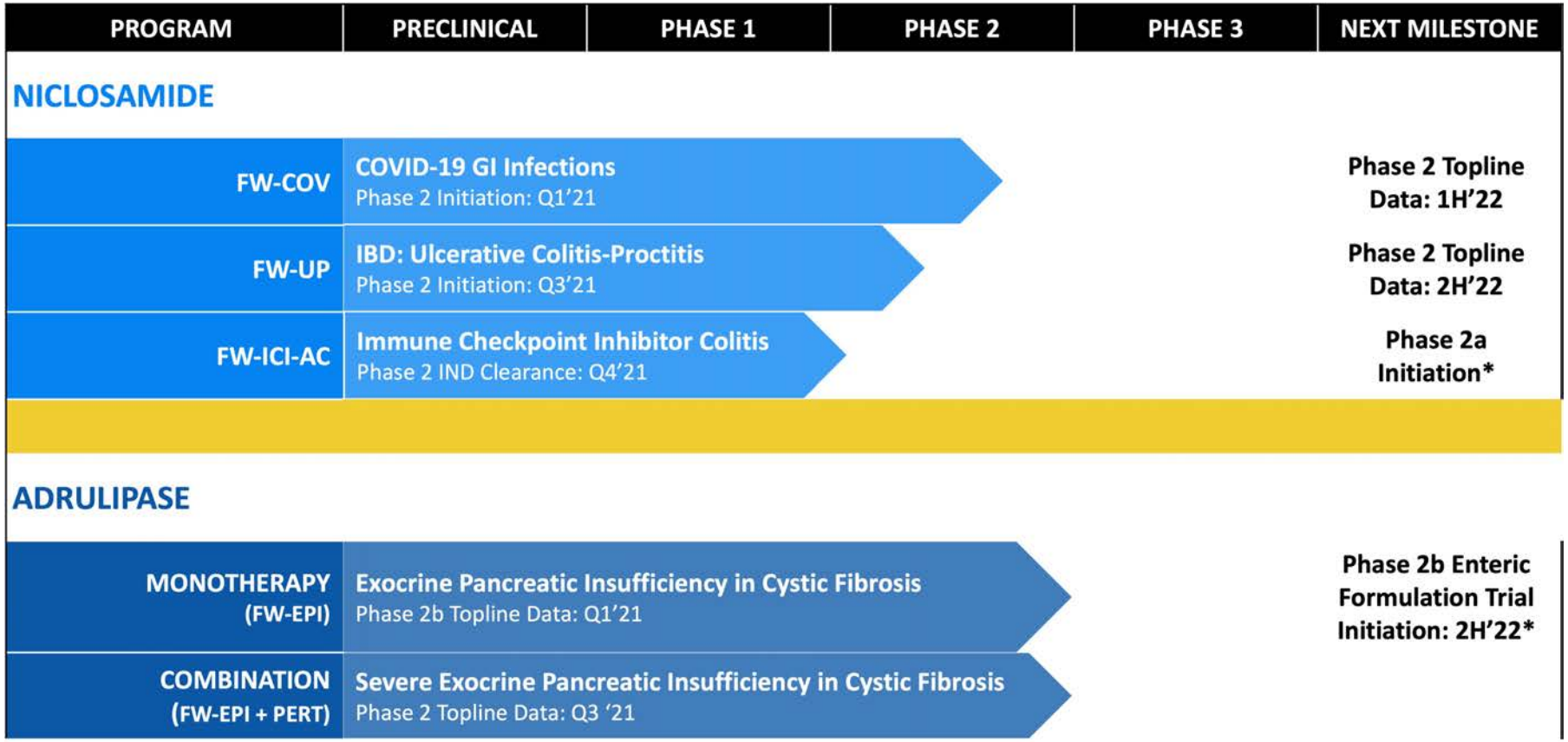
- Led successful registration efforts for 12 BLA/NDA submissions in the U.S. and 10 in Europe and Asia.
- 10 years on Harvard Medical School faculty



Daniel Schneiderman
Chief Financial Officer

Biophytis LIVE HEALTHIER LONGER
MetaStat
BHP Burnham Hill Partners LLC Investment & Merchant Banking
HCW H.C. WAINWRIGHT & CO.

First Wave BioPharma Pipeline: Four Clinical Stage Programs in 2022



* Anticipated

Expanding the GI Portfolio into IBD
Multi-Billion Dollar Opportunities with Mild-to-Moderate Patients

	Prevalence	Market Size
COVID-19 GI Infections	• ~20% Acute COVID • ~ 50% all patients have virus in GI tract • ~50% Long COVID	~$20 Billion COVID anti-virals
Ulcerative Colitis (Mild-Moderate)	• 830,000 UC patients (U.S.) • 700,000 (84%) mild-moderate	$5 Billion UC $4.6 B Mild-to-Moderate
Immune Inhibitor Checkpoint – Associated Colitis	• ~300,000 patients eligible for ICIs (U.S.) • ~30% of ICI patients develop diarrhea • ~7500-15,000 patients develop ICI-AC	Potential Orphan Designation
Exocrine Pancreatic Insufficiency	• 30,000 CF (U.S.); 100K (WW) • 90,000 CP (U.S.); 4x^{+} (WW)	>$2.2 Billion Global PERT >$1.6 Billion U.S. PERT

Sources:
COVID: *Acute COVID: (35) Gut Journal: Vol 69, Issue 6: 2020; (36) Gut Journal: Vol 69, Issue 6: 2020; (37) JAMA Network: Vol 3, Issue 6: 2020; (38) Lancet Gastroenterol Hepatol: Vol 5, Issue 5: 2020; (40) Cheung Gastroenterology: Vol 159, Issue 1: 2020. Long COVID: Davis, Hannah E, Assaf, Gina S, et al. "Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact". medRxiv. https://www.medrxiv.org/content/10.1101/2020.12.24.20248802v3 Dec. 27, 2020.; New York Times. (9/5/21) https://www.nytimes.com/interactive/2021/world/covid-cases.html ; https://www.businesswire.com/news/home/20210210005504/en/Global-Anti-Viral-Drug-Therapy-Market-2020-to-2030---Opportunities-and-Strategies-with-COVID-19-Implications-and-Growth---ResearchAndMarkets.com*
ICI-AC: Wang DY, Ye F, Zhao S, et al. Incidence of immune checkpoint inhibitor-related colitis in solid tumor patients: a systematic review and meta-analysis. *Oncoimmunology* 2017; 10: e1344805; Immune Checkpoint Inhibitors Market, ResearchAndMarkets.com, 2020.
UC: *GlobalData Ulcerative Colitis Global Drug Forecast and Market Analysis to 2026: US Adults. 2018*
EPI: The CorStar Group 2019. Cystic Fibrosis Foundation 2020. National Pancreas Foundation 2020.

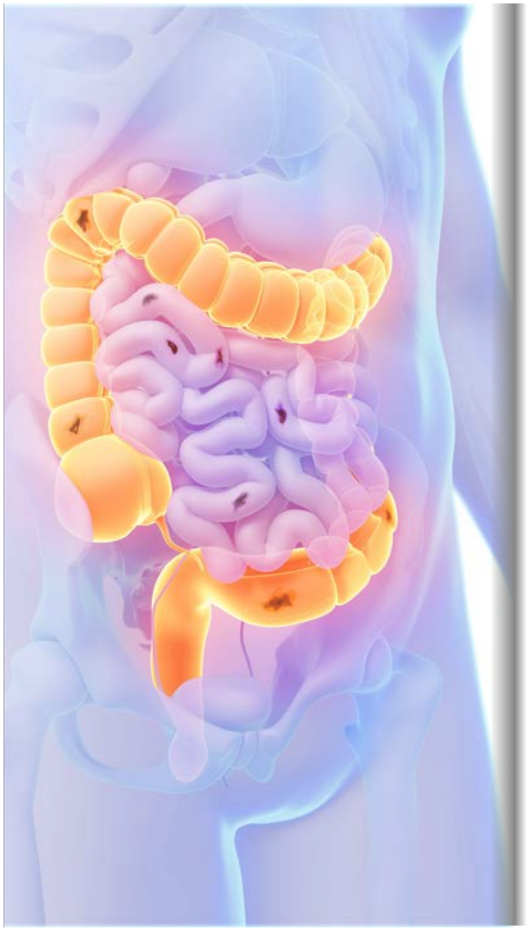
First Wave BioPharma

NICLOSAMIDE:

- COVID-19 GI Infections
- IBD: Ulcerative Colitis-Proctitis
- Immune Checkpoint Inhibitor - Associated Colitis

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



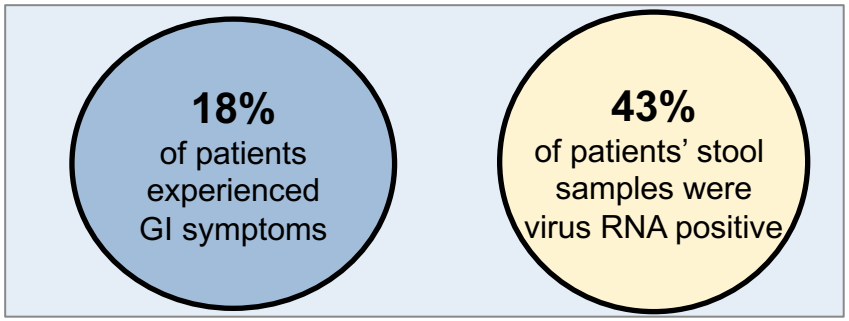
Proprietary Micronized Formulations: Potentially Transformative Efficacy

- **Micronized niclosamide – a transformative treatment for multiple GI indications:**
  - Reduced particle size (~7 μm) compared to regular non-micronized (~60 μm) niclosamide
  - Smaller particles have greater surface to solvent (GI fluids) ratio
  - Improved dissolution: broader distribution and higher local GI concentrations
  - Not systemically absorbed
  - Preclinical studies confirm higher GI concentrations (~200x) with micronized niclosamide
- **Micronized formulation, similar to non-micronized niclosamide, is not systemically absorbed (animal studies)**
  - **Historically clean safety profile**
    - Avoids steroid-related complications; non-immunosuppressant

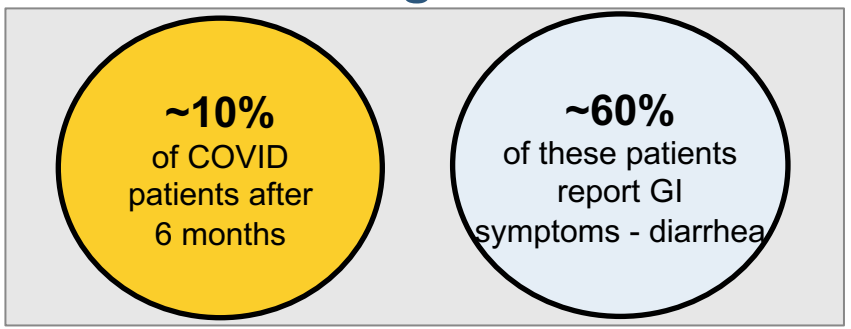
FW-COV: Treating COVID-19
GI Infections

COVID-19: The Medical Problem of our time
Urgent Need for Treatment of Acute and Long COVID-19 GI Infections

Acute COVID



Long COVID



- Gastrointestinal Infections with COVID-19:
  - Symptoms include severe diarrhea, vomiting, and abdominal pain
  - Possible reservoir for recurrence and/or fecal spread
  - ACE2, entry receptor for COVID-19, is highly expressed on GI cells
- No treatment for COVID diarrhea currently available
- Urgent need to reduce hospital burden of patients and potential hospital spread

The Potential Solution: A targeted drug to destroy COVID-19 in the gut that is fast-acting and can be administered in an out-patient setting

Sources: Acute COVID: (35) Gut Journal: Vol 69, Issue 6: 2020; (36) Gut Journal: Vol 69, Issue 6: 2020; (37) JAMA Network: Vol 3, Issue 6: 2020; (38) Lancet Gastroenterol Hepatol: Vol 5, Issue 5: 2020; Wong, M, et. al. "Detection of SARS-CoV-2 RNA in fecal specimens of patients with confirmed COVID-19: A meta- analysis". Journal of Infection 81 (2020) e31-e38; Doorn, A. "Systematic review with meta-analysis: SARS-CoV-2 stool testing and the potential for faecal-oral transmission." Alimentary Pharmacology & Therapeutics. 2020: 52:1276-1288.*35(40) Cheung Gastroenterology: Vol 159, Issue 1: 2020.Long COVID: Davis, Hannah E, Assaf, Gina S, et al. "Characterizing Long COVID in an International Cohort: 7 Months of Symptoms andTheir Impact". medRxiv. https://www.medrxiv.org/content/10.1101/2020.12.24.20248802v3 Dec. 27, 2020.*

Micronized Niclosamide: The Potential Key to Killing COVID-19 in the GI Tract

Advantages of Micronized Niclosamide for Treatment of COVID-19 Diarrhea:

- Niclosamide: Best activity against COVID-19 in Institut Pasteur Korea screen
- Mechanism of Action: Induces ‘autophagy’ in COVID-infected cells, reduces COVID propagation
- Local GI niclosamide concentration now reaches levels needed to kill COVID-19 (confirmed in animal study)
- Animal study shows micronization does not lead to systemic absorption
- Low COGS and scalable manufacturing are attractive

COVID GI Infection: Reservoir Trial

- Phase 2 Reservoir trial initiated in April 2021

- Fully Enrolled January 2022
  - No Safety issues related to niclosamide

- Topline data anticipated in 1H 2022

- Potential Emergency Use Authorization (EUA)

Reservoir

IBD Opportunity:
Ulcerative Colitis-Proctitis

Ulcerative Colitis

- Affects ~830K people in the U.S.[1]

- Five major types of Ulcerative colitis (UC)
  - **Ulcerative Proctitis**
  - **Proctosigmoiditis**
  - Left-sided Colitis
  - Pancolitis
  - Acute Severe Ulcerative Colitis

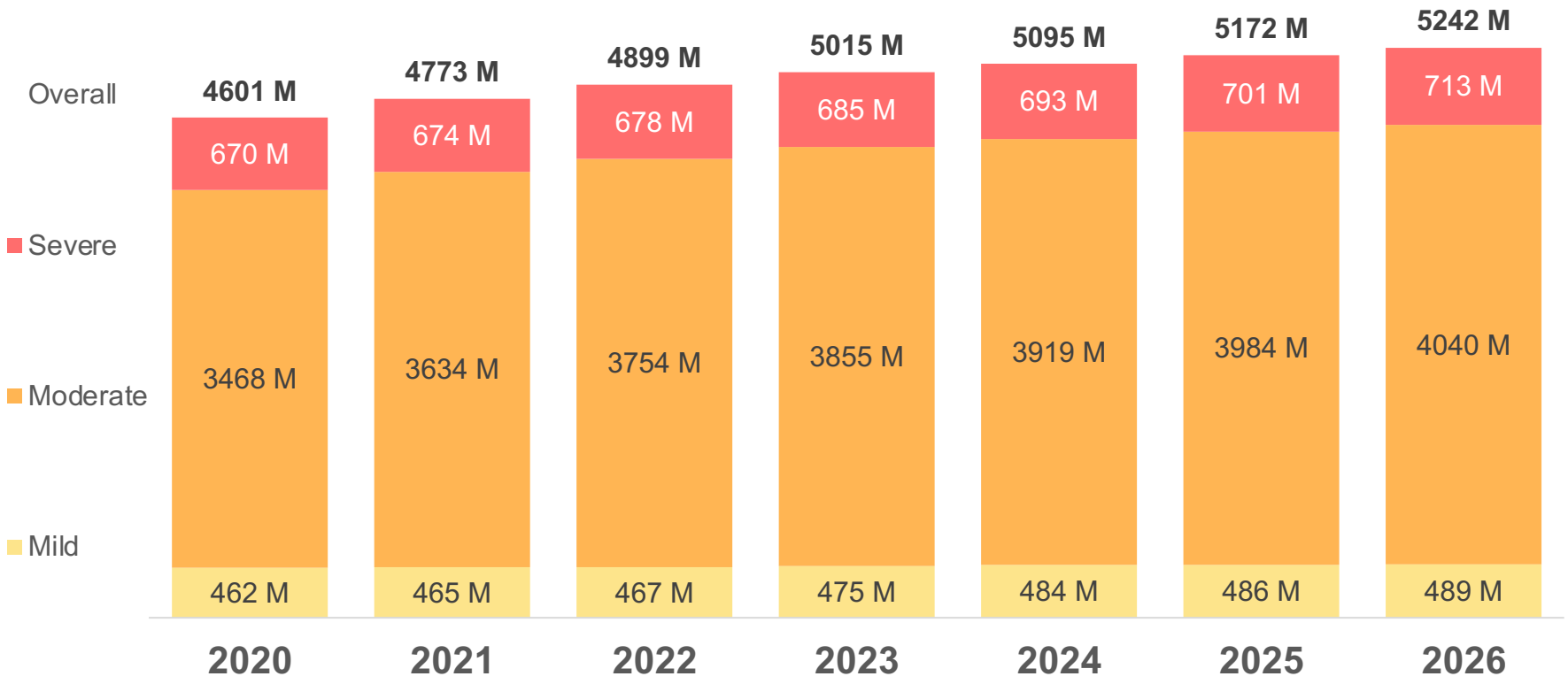
- Therapies
  - Mild disease: sulfasalazines; 5-ASAs (mesalamine)
  - Moderate: steroids (budesonide; prednisone); azathioprine; 6-mercaptopurine; methotrexate
  - Severe: Anti-TNF; Entyvio; Xeljanz; Stelara

Source: (23) GlobalData Ulcerative Colitis Global Drug Forecast and Market Analysis to 2026: US Adults. 2018.

Ulcerative Colitis: The launch of new novel medications for the treatment UC is the primary driver in the expected increase in sales

Market Projections: Ulcerative Colitis Sales by Severity (in dollars)[23]

(Estimated sales of ulcerative colitis medications for American adults by severity year over year)



Source: (23) GlobalData Ulcerative Colitis Global Drug Forecast and Market Analysis to 2026: US Adults. 2018.

Mild to Moderate Prevalence is 84% of all UC Patients; 86% of UC Market Size

Many Patients with Mild-to-Moderate UC Have Inadequate Response to First Line Therapy

Mild-to-Moderate UC

DIAGNOSIS

Doctors diagnose patient with mild-to-moderate UC

TREAT

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

FAIL

Remission fails to occur in patients all too often

*~58% fail remission with oral 5-ASA**

*~50% fail remissio n with rectal 5-ASA**

TREAT 2nd LINE

An early, effective 2nd line treatment may prevent damage and in some cases stop disease progression

Moderate-to-Severe UC

NEXT STEPS

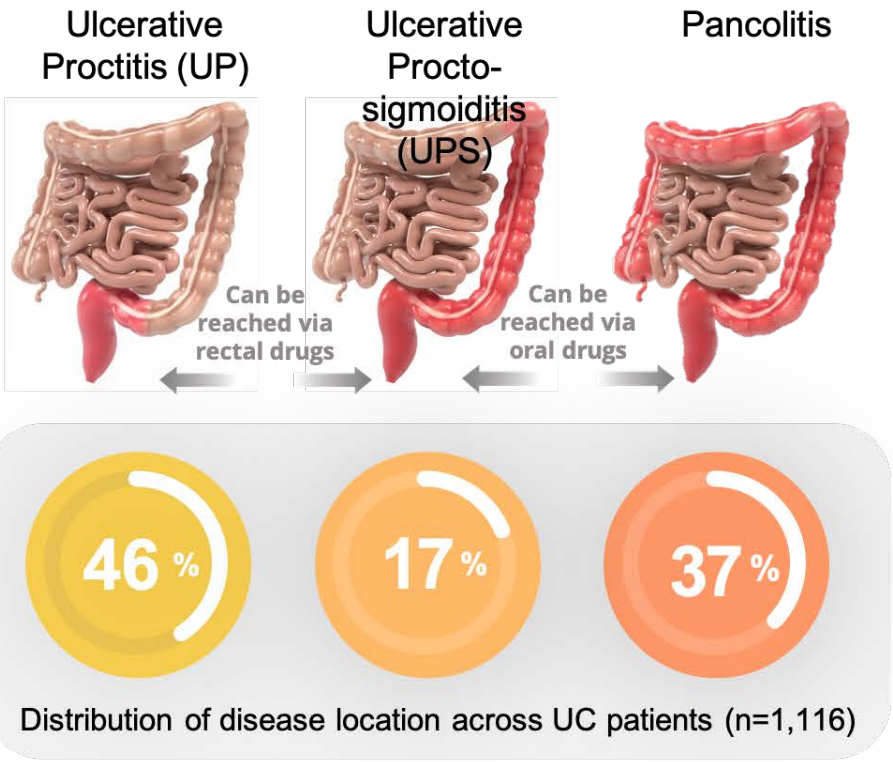
- Treated with corticosteroids, anti-TNF therapy, or other agents
- All have significant systemic side effects

SURGERY

Colectomy (a major surgical procedure) to treat the disease

Rationale for Conducting Initial Proof-of-Concept in UC

- Lower placebo response rate vs. Crohn's disease
- UC is easily monitored by serial endoscopy, which provides objective endpoints
- Significant unmet medical need, particularly in patients that fail 5-ASA
- >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**



Role for Niclosamide in IBD

- Pharmacology ideal for local bowel disease; not absorbed from GI tract
- Mechanism of action is to impair oxidative phosphorylation; i.e. how cells make energy.
- Pathogenic Th17 cells have overly active oxidative phosphorylation; niclosamide down regulates this overactive cell.
- Data from Phase 1b study of niclosamide in ulcerative proctitis show promising results

Ulcerative Colitis – Proctitis: Clinical remission efficacy with topical rectal niclosamide formulation superior to budesonide in Low Dose Phase 1b Trial

- Clinical remission efficacy of **59%** compares favorably to steroids as 2nd line therapy in mild-to-moderate Ulcerative Colitis (UC)
- Remission rate for budesonide in Ulcerative Proctitis (UP)/Ulcerative Proctosigmoiditis (UPS) is **38-44%**
- Steroid use lowers patients' ability to fight infections and leads to complications including bleeding, nausea, heartburn, and headaches
- Treatment-emergent adverse event (TEAE) reported in 35% (6/17 subjects)
  - All but 1 TEAE was mild
- No serious or drug-related TEAEs

First Ever Proof of Principle for Treatment of IBD with Niclosamide

First Wave BioPhase Phase 2a Trial of Ulcerative Colitis - Ulcerative Proctitis/Sigmoiditis

- **Stage 1: Lower Dose Completed**
  - 17 patients
  - Relapsed on 5-ASA first line therapy
  - Modified Mayo Score (MMS) 4 to 7
  - Treat for 6 weeks with niclosamide enema, **150 mg**, twice daily
  - Key endpoints: Safety, Clinical remission (MMS = or < 2)

- **Stage 1: Results**
  - 10/17 achieved clinical remission (59%)
  - Well-tolerated
  - Biomarkers consistent with clinical response

- **Stage 2: Higher Dose Initiated**
  - 32 patients (28 patients placebo controlled)
  - Relapsed on 5-ASA first line therapy
  - MMS 4 to 7
  - Treat for 6 weeks with niclosamide enema, **450 mg**, twice daily vs Placebo enema twice daily
  - Key endpoints same as for Stage 1
  - **Niclosamide shown to be well-tolerated in the first four patients in the higher-dose cohort**

Ulcerative Colitis - UP/UPS: Next Steps

- End of Phase 2 Meeting with FDA

- U.S. FDA IND submission

- Phase 2b trial
  - Placebo Controlled, three arms
  - Placebo vs 150 mg vs 450 mg
  - Induction treatment phase, 6 weeks
  - Maintenance treatment phase for responders, 6 months

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

ADRULIPASE: FW-EPI Clinical Program

Recombinant lipase for treatment of Exocrine Pancreatic Insufficiency (EPI)

- 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

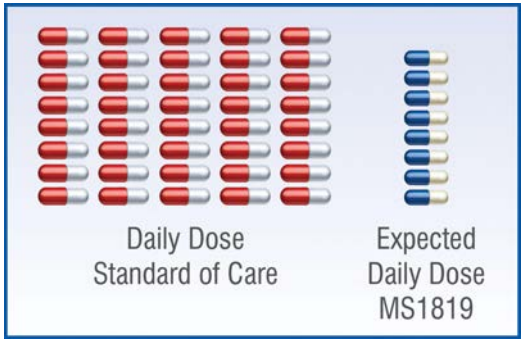
- Topline Phase 2b CF monotherapy data announced in Q1 2021
- Topline Interim Phase 2 CF combination (MS1819 + PERT) therapy data announced in Q3 2021; final Clinical Study Reports in Q4 2021

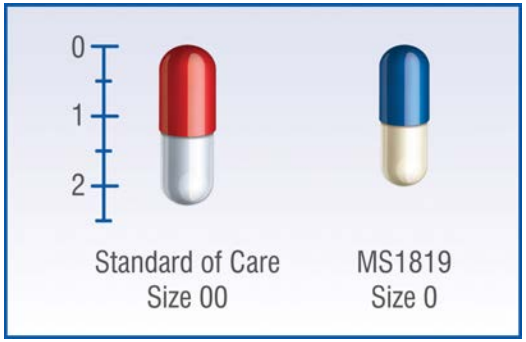
New enteric granule formulation being developed, Phase 2b trial anticipated in 2H 2022

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

Adrulipase: Fulfilling an Unmet Medical Need

	PERT	MS1819
Drug Substance	**Porcine-derived** pancreatic enzyme replacement therapy (PERT)	**Recombinant yeast** (*Yarrowia lipolytica*) lipase-derived replacement therapy
Stability in Acidic GI Environment	**Limited**	**More stable**
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)**	**8-16 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.

Lessons Learned From the MS1819 Program and Next Steps

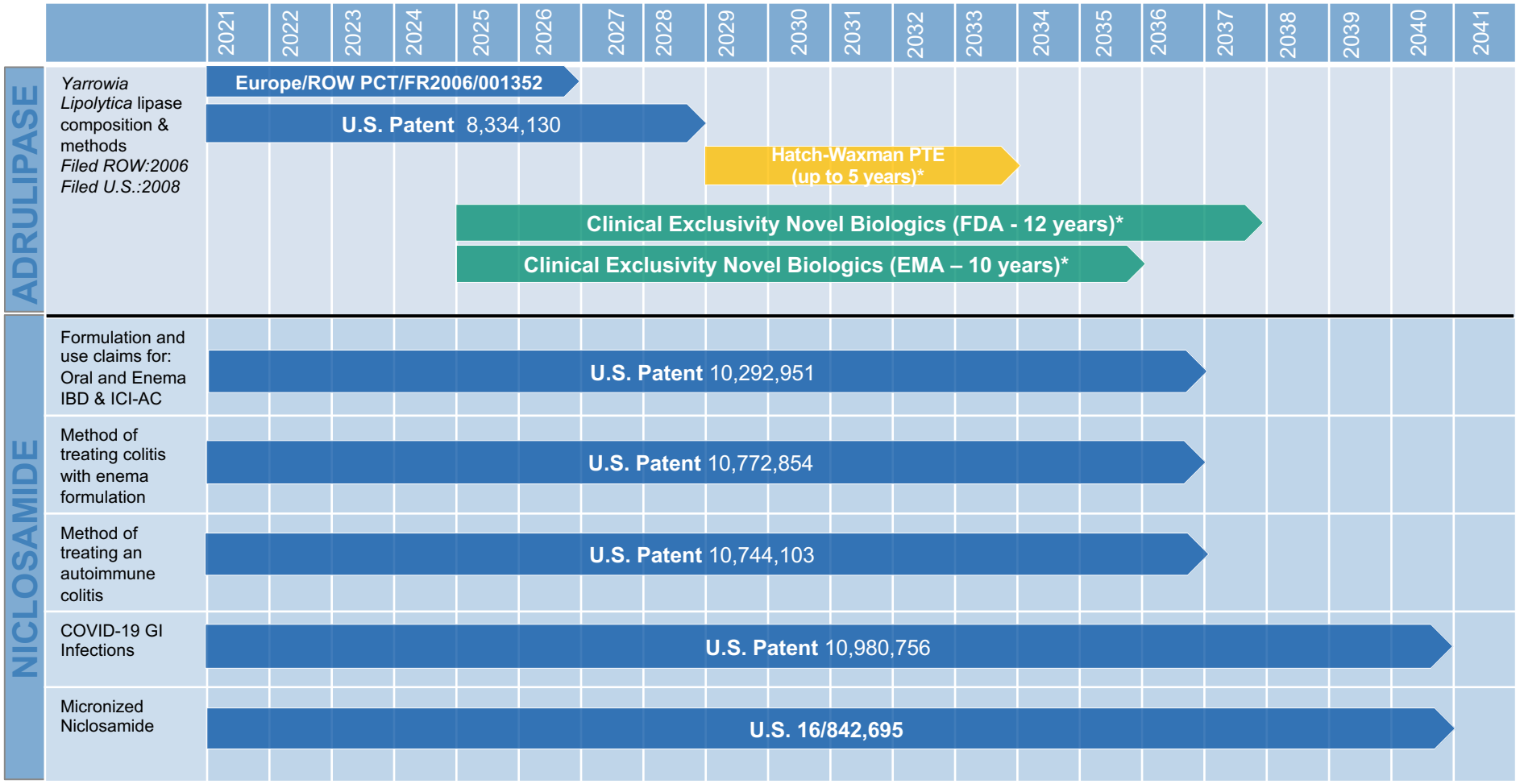
- Four Phase 2 Studies to Date:
  - Phase 2 CP
  - Phase 2a CF Monotherapy (OPTION)
  - Phase 2b CF Monotherapy (OPTION 2)
  - Phase 2 CF Combination Therapy (MS1819 + PERT)
- Product has evidence of lipase activity
- Product shows dose-response in chronic pancreatitis
- Combination therapy with commercial 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%
- Current powder formulation in immediate release or enteric capsules is not sufficient to obtain consistent CFAs >80%
- Formulation with good gastric dispersion plus gastric acid protection logical next step

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

First Wave BioPharma

- Intellectual Property
- Financial Overview
- Investment Highlights

Robust IP Portfolio (2021-2041)
Key Patents Secure for the next 15-20 years



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Financial Overview

Nasdaq	FWBI	Cash & Cash Equiv.	$7.1 MM(2)
Stock Price	$1.66(1)	Enterprise Value	$23.1 MM(1)
Common Shares Outstanding	14.9 MM	Shares Out/Fully Diluted	21.8 MM(3)
Market Cap	$24.7 MM(1)	Avg. Daily Volume (3 months)	1.61 MM
Preferred Stock (SV) (CP: $7.70)	$5.6 MM(1)	Avg. Daily Volume (10 days)	1.65 MM
Debt	$0	Full-Time Employees	16

(1) As of market close 1/3/2022
(2) As of 9/30/2021 (Form 10-Q filled 11/15/2021). Does not include $10.0 MM of net proceeds raised subsequent to 9/30/2021.
(3) Includes 721 K shares issuable upon conversion of Series B Preferred Stock at $7.70/share; 5.4 MM shares issuable upon exercise of warrants (WAEP: $9.73); 770 K shares issuable upon exercise of options (WAEP: $7.33).

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