



Processa Pharmaceuticals

**Clinical Pipeline Update**  
**March 30, 2022**

# Disclaimer: Forward Looking Statements

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# Processa Highlights

- **Development Company Focused on Improving the QOL or Survival of Patients with an Unmet Medical Need**
  - Present programs represent 5 different U.S. markets with potential sales of > \$1.0 B for each drug
  - Each drug has the potential to expand into additional markets
- **Management & Development Team with Track Record of Success; 2022 Capital Efficient with SG&A ~ \$4M/Year**
- **Regulatory Science Approach to Drug Development Initially Developed during FDA Collaborations 30 Years Ago and Refined over Time**
- **Continually Evaluating Approaches to Expedite Development (e.g., Trial Design, FDA Interactions, FDA Expedited Programs such as Fast Track, Breakthrough, Accelerated Approval)**
- **Near Term Milestones (March-August)**
  - Next Generation Capecitabine: Re-start Phase 1B trial and determine the PCS6422 regimen to inhibit DPD activity for the 7 days of capecitabine dosing
  - PCS499: Complete enrollment of patients for interim analysis
  - PCS12852: Enroll the first patient in Phase 2A gastroparesis trial
  - PCS3117: Complete initial development of biomarker assays
- **End of Year Milestones (September–December)**
  - Next Generation Capecitabine: Complete enrollment of Phase 1B trial and obtain preliminary Maximum Tolerated Dose (MTD) for capecitabine
  - PCS499: Complete enrollment of patients for trial and obtain top-line results on interim analysis
  - PCS12852: Complete enrollment of patients in Phase 2A trial
  - PCS3117 & PCS11T: Define potential development programs for approval in multiple cancers
- **2023 Milestones U.S.**
  - Obtain final results from 3 clinical trials, 3 different indications; initiate 2 new trials (pivotal registration and/or Phase 2B trials)

# Processa's Risk Abated Approach and Criteria for Drug Selection

Experience in Adding Value to Companies: > 30 FDA Approvals & Regulatory Science Contracts from FDA

DEVELOP NOT DISCOVER



REGULATORY SCIENCE PLATFORM

Unmet Medical Need + Efficacy Evidence + Regulatory Science + Capital Efficiency + Potentially High ROI

- Clear and obvious **patient need**
- **Favorable competitive** dynamics

- **Evidence of clinical efficacy** in targeted medical condition
- **Higher** probability of **successful development**






- **Improve Benefit/Risk** profile that FDA evaluates for approval
- **Optimize trial design** and **anticipate** what **FDA** requires for approval (Trifecta: decreasing risk, time to approval & cost)

- **Leverage** considerable **prior investments** before licensing (tox, CMC, etc.)
- **Efficient development** program and clinical trial design

- **Intelligently monetize and partner assets**

# Pipeline With High Value 2022 Milestones

## Five Drugs Each with \$1B Market Opportunity

Drug	Disease Target	Non-clin	Phase 1	Phase 2	Phase 3	Status	2022 Milestones
Next Generation Capecitabine Phase 1B (PCS6422)	Metastatic Colorectal, Breast, Other Cancers					Cohort 1&2 no DLTs; 6422 Regimen Alters 5-FU Metabolism for 1-2, not 7 Days; Modified Protocol Submitted to FDA	<a href="#">1H'22</a> - Restart Phase 1B, Identify 6422 Regimen; <a href="#">2H'22</a> - Complete Enrollment, Preliminary Identification of Capecitabine MTD
PCS499 Phase 2B	Ulcerative Necrobiosis Lipoidica					3 Patients Dosed; 2 Patient in Pre-Screening; Adding Sites	<a href="#">1H'22</a> - Complete Interim Group Enrollment <a href="#">2H'22</a> - Interim Analysis, Complete Enrollment
PCS12852 Phase 2A	Gastroparesis, Constipation Disorders					Activating Trial Sites; Screening Patients	<a href="#">1H'22</a> - FPI Phase 2A; <a href="#">2H'22</a> - Complete Enrollment
PCS3117 Phase 2B	Pancreatic, Other Cancers					Biomarker Assay Started; Development Programs Being Evaluated	<a href="#">1H'22</a> - Complete Initial Development of Biomarker Assays, <a href="#">2H'22</a> - Define Possible Paths-Clinical Trials to FDA Approval
PCS11T Pre-IND	SC Lung, Other Cancers					Manufacturing Sites Being Selected, Assessing Regulatory Development Paths	<a href="#">2H'22</a> - Select Manufacturing Sites; Define Possible Paths-Clinical Trials to FDA Approval

FPI – First Patient In (i.e., randomized)

MTD – Maximum Tolerated Dose

Blue - Use of Existing Cash



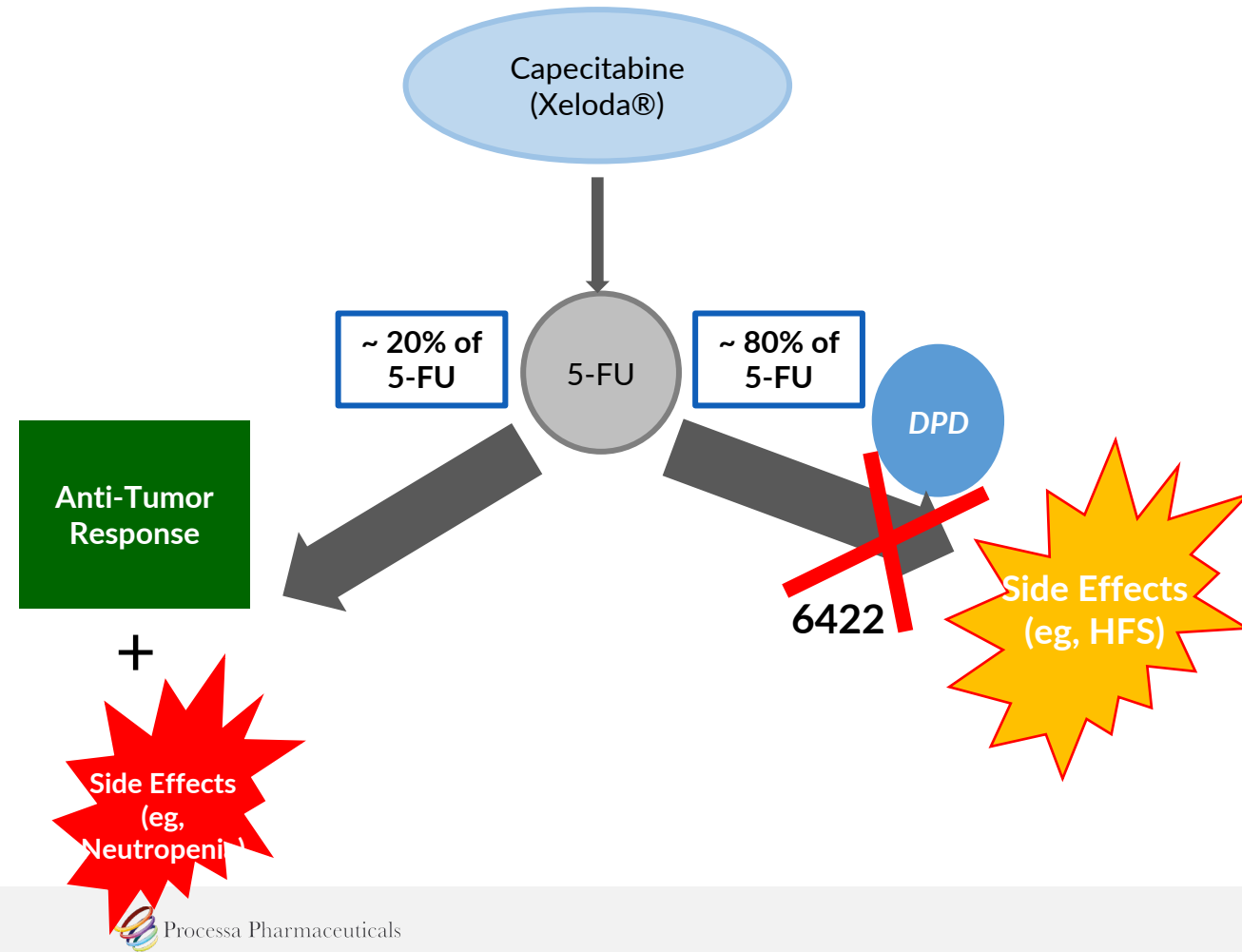
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**Next Generation Capecitabine  
(Combination of Capecitabine with PCS6422)**

**Metastatic Colorectal Cancer, Breast Cancer,  
Pancreatic Cancer, Other Cancers**

# Next Generation Capecitabine (PCS6422 and Capecitabine) > \$1B Market

**When PCS6422 Irreversibly Inhibits DPD,  
Next Generation Capecitabine Should be  
More Potent Than FDA Approved  
Capecitabine**



## 2021 Cohort 1 and 2 Interim Results

- No DLTs, no drug-related adverse events greater than Grade 1, and no hand-foot syndrome side effects were observed in Cohort 1 and 2
- Next Generation Capecitabine with 1 dose of PCS6422 inhibited DPD activity 24-48 hours after PCS6422 administration to < 10% of 5-FU metabolized to FBAL compared to 80% reported for FDA approved capecitabine
- 24-48 hours after PCS6422 administration, 5-FU potency, based on systemic exposure per mg of capecitabine, was **at least 50 x greater** than reported for FDA approved capecitabine
- The improved metabolism profile and increased **potency did not exist 7 days after a single dose of PCS6422**; the Phase 1B protocol and PCS6422 dosage regimen has been modified

# Next Generation Capecitabine

✓ Response Rate

✓ Survival Time

✓ HFS Rate &/or Severity

✓ % Treatment Resist. Pts

- Need to identify a regimen of 6422 that provides minimum exposure to 6422 while still inhibiting 5-FU metabolism such that  $< 10\%$  of 5-FU is metabolized to FBAL throughout capecitabine dosing
- Since 6422 irreversibly inhibits the DPD enzyme, metabolism to FBAL after 6422 administration could occur from some DPD not being inhibited and/or the formation of new DPD molecules
- The timeline of DPD inhibition and de novo formation needs to be evaluated in order to identify 6422 regimens that will inhibit DPD throughout capecitabine dosing



# 2022 Milestones - Next Generation Capecitabine Colorectal Cancer

## Phase 1B Clinical Trial

- Modified Phase 1B protocol to determine the dosage regimen of 6422 that will minimize 6422 exposure while still inhibiting DPD to  $< 10\%$  of normal activity over all 7 days of capecitabine dosing
  - Evaluating the timeline of DPD enzyme inhibition and de novo formation
  - Evaluate the possibility of using an Individualized/Personalized Treatment approach
- Re-activating all previous sites; adding 1-2 more sites
- Sites with IRB approval have begun to identify patients; expect to restart dosing in 2Q'22;
- Initial evaluation of DPD timeline should occur June/July; preliminary determination of MTD of Next Generation Capecitabine should occur in 4Q'22 since the study is open labeled

## Development and Regulatory

- Evaluate how an Individualized/Personalized Treatment approach can be added to the development program if the Phase 1B evaluation proves positive for this approach
- Interact with the FDA to define regulatory approaches to expedite the development
- The overall timeline for initiation of a pivotal registration trial (2023-2024) and NDA submission (2027-2028) is not expected to change



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**PCS499**

**Ulcerative Necrobiosis Lipoidica (uNL)**

# PCS499: First Drug to Treat Ulcerative Necrobiosis Lipoidica (uNL)

- Skin and tissue below the skin becomes necrotic forming open ulcers; can last from months to years with complications such as infections, amputation, and cancer
- Literature reports approximately 22,000 – 55,000 uNL patients in U.S. with painful ulcers occurring naturally or from contact trauma to the lesion (numbers may actually be significantly less but should not alter \$1B market potential given the flexibility in pricing as the only approved treatment)
- Natural complete healing or wound closure of moderate to severe ulcers during the first 1-2 years after onset occurs in less than 5% of these patients

**Severe NL**

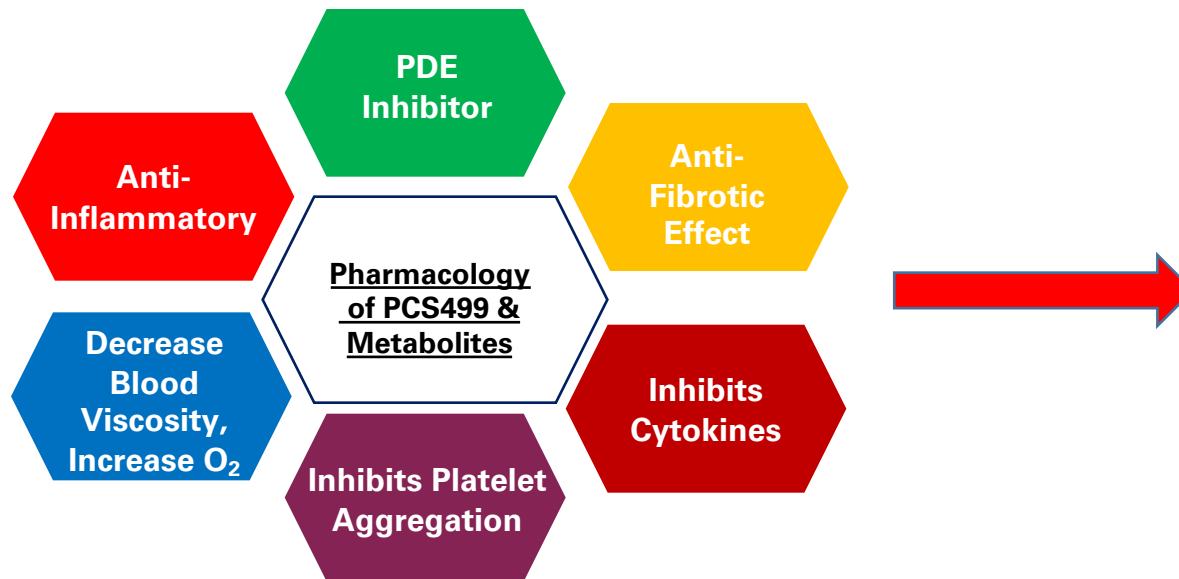


**Mild NL**



# Unmet Medical Need, Evidence of Clinical Efficacy

- No FDA approved treatment for uNL or NL, no standard of care, all treatments are inadequate
- Drugs have been used off-label with mixed success (e.g., pentoxifylline (PTX)); provide poor safety profile given their limited efficacy
- PCS499 is the deuterated analog of a major metabolite of PTX; has identical metabolites and pharmacological targets but PK of 499 and its metabolites is different than PTX and its metabolites resulting in a better 499 safety profile and allowing for the administration of a higher, more efficacious dose of 499
- Pharmacological targets of 499 and its metabolites positively affect 6 of the 7 pathophysiological changes that can occur with NL

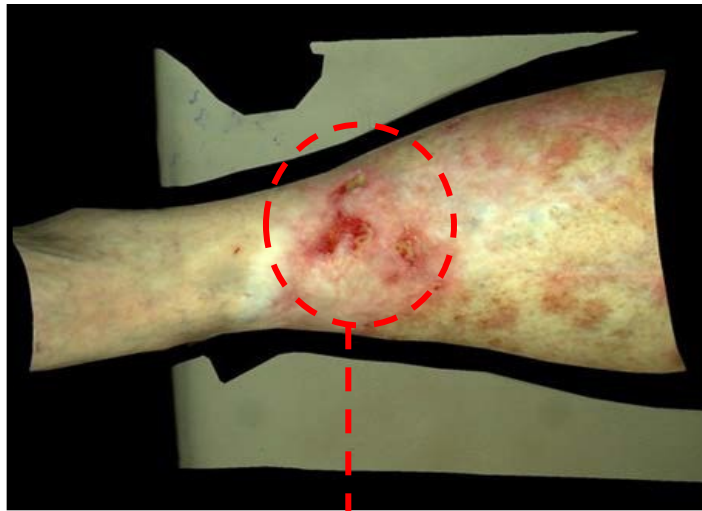


## Pathophysiological Changes in NL

- Decrease in blood flow & Oxygenation
- Decrease in platelet survival
- Increase inflammation
- Increase fibrosis
- Increase cytokines
- Degeneration collagen
- Alters fat deposition

## PCS499 in 2020 - 2021

- Determined 1.8 gm/d of 499 was safe and effective in closing the open ulcer of the 2 patients with uNL in an open-labeled Phase 2A trial



**Baseline**



**Complete Closure**

- Continued communications with FDA to define uNL as a serious condition
- Collaborated with FDA to define the information needed from a Phase 2B trial to guide us in the design of a single pivotal Phase 3 trial in 2023
- Initiated the Phase 2B trial in uNL

# 2022 Milestones – PCS499 in uNL

## Phase 2B Clinical Trial

- 3 patients enrolled; preliminary results show ulcers closed in some patients; 2 patients in pre-screening
- Although patients have been identified in pre-screening (identified through pictures to have an ulcer(s)) and expressed interest in being screened, COVID has affected enrollment given co-morbidities of these patients (patients in pre-screen have died from COVID, patients identified not willing to travel)
- In 4Q'21 began putting in place remedial efforts to increase patient enrollment; efforts still ongoing
- Replaced ex-US sites not successful in enrolling patients with 2-4 new US and/or new ex-US sites
- Evaluating if the questions that the Phase 2B trial is addressing can be answered with fewer patients in the interim and final analysis
- Interim analysis group of patients should be enrolled by 6/30/22 with the interim results expected December 2022; complete enrollment of study by end of year

## Development and Regulatory

- Prevalence of uNL likely much less than the literature estimate of 22,000 – 50,000 patients
- Plan for pivotal trial 2H'2023
- Given prevalence may be lower than reported, multiple possible drug development “roadmaps” to approval are being defined with plans to discuss approaches with the FDA in 2022-2023



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**PCS12852**

**Gastroparesis**

# Gastroparesis

## PCS12852 is a More Potent and More Selective 5HT<sub>4</sub> Agonist than Previous 5HT<sub>4</sub> Agonists

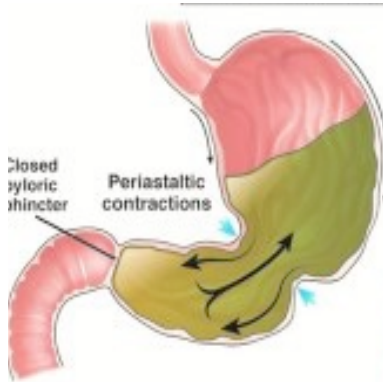
### ➤ Target Indication:

- Treatment of moderate to severe gastroparesis

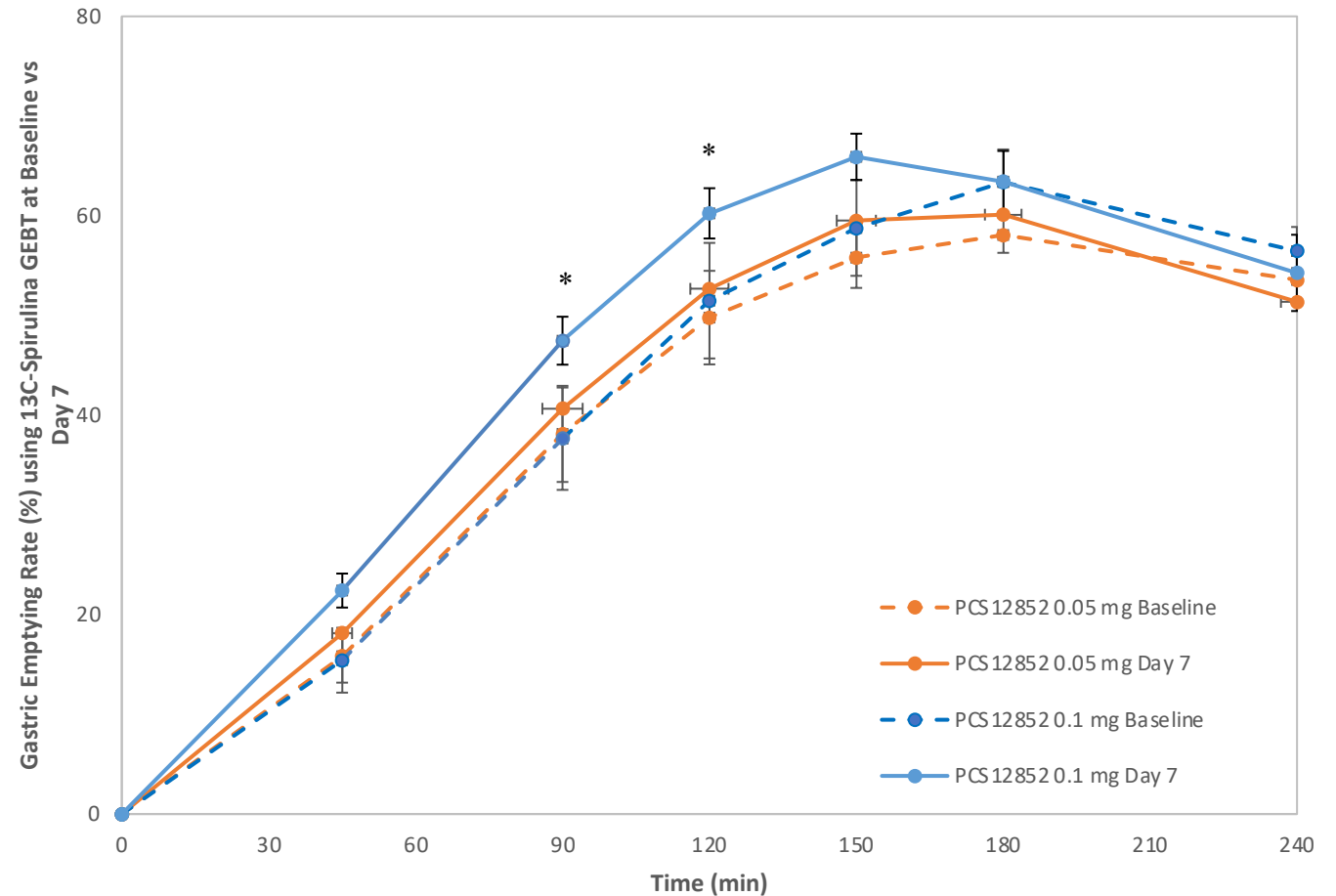
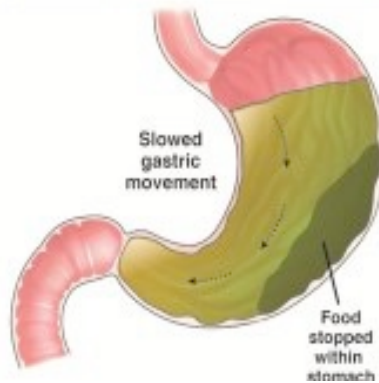
### ➤ Target Claims:

- Improves gastric emptying rate and the symptoms associated with moderate to severe gastroparesis (e.g., bloating, pain, nausea, vomiting)

Normal Gastric Emptying



Gastroparesis





# Treatment of Gastroparesis (> \$1.5B Market)

- Existing FDA approved drugs and off-labeled prescribed drugs are mainly used for the treatment of diabetic gastroparesis
- All these drugs have a poor side effect profile limiting their use
- Present market size for gastroparesis is estimated to be over \$1.5B

	<b>PCS12852</b>	<b>Other 5HT4 Drug (e.g., Cisapride, Prucalopride, Mosapride)</b>	<b>Dopamine D2 Antagonist (e.g., Metoclopramide)</b>
Target Population	<ul style="list-style-type: none"><li>• Potentially all gastroparesis patients (e.g., diabetic, idiopathic)</li></ul>	<ul style="list-style-type: none"><li>• Diabetic gastroparesis patients</li></ul>	<ul style="list-style-type: none"><li>• Diabetic gastroparesis patients</li></ul>
Binding	<ul style="list-style-type: none"><li>• Specific &amp; potent 5HT4 receptor binding</li></ul>	<ul style="list-style-type: none"><li>• Less specific binding to 5HT4 than 12852</li><li>• Less potent than 12852</li></ul>	<ul style="list-style-type: none"><li>• Binds to Dopamine D2 receptors</li></ul>
Side Effects	<ul style="list-style-type: none"><li>• No serious side effects in clinical studies to date</li></ul>	<ul style="list-style-type: none"><li>• Serious cardiovascular side effects (e.g., cisapride removed from market)</li><li>• Suicidal ideation (e.g., prucalopride)</li></ul>	<ul style="list-style-type: none"><li>• Black Box Warning serious neurological side effects, Side effects require limited use</li></ul>
Efficacy	<ul style="list-style-type: none"><li>• Increase gastric emptying rate in patients with constipation</li></ul>	<ul style="list-style-type: none"><li>• Increase gastric emptying rate</li><li>• Successful treatment demonstrated</li></ul>	<ul style="list-style-type: none"><li>• Only drug FDA approved for treatment of gastroparesis</li></ul>

# 2022 Milestones – PCS12852 in Gastroparesis

## Phase 2A Clinical Trial

- 12852 Phase 2A is a placebo-controlled, randomized, dose-response trial evaluating the gastric emptying rate and gastroparesis symptoms in patients
- Site activation of 9 sites and patient screening at IRB approved sites has started
- Screen failure rate is estimated to be approximately 50%
- FPI for Phase 2A expected 2Q'22 with completion of study conduct 4Q'22
- Final analysis of Phase 2A expected Dec 2022-Jan 2023

## Development and Regulatory

- Primary endpoints for pivotal trials will be based on symptoms
- Evaluating alternative regulatory paths to expedite approval with plans to discuss approaches with the FDA in 2022-2023
- Phase 2B trial to begin in 2023



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**PCS3117**

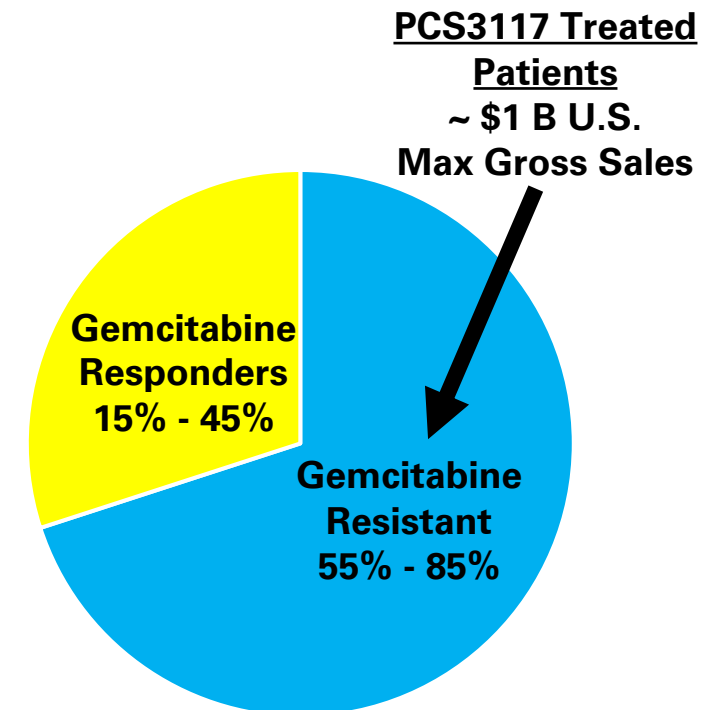
**Metastatic Pancreatic Cancer, Biliary Cancer, Other  
Cancers**

**PCS11T**

**Small Cell Lung, Pancreatic, Colorectal, Other  
Cancers**

# PCS3117 for Cancer Patients Resistant to Gemcitabine

- PCS3117 has a similar structure to gemcitabine but is activated through a different pathway and causes cancer cell apoptosis in more ways than gemcitabine
- PCS3117 has been shown in gemcitabine resistant cancer patients and tumor animal models to alter cancer progression
- Gemcitabine is the most widely used chemotherapeutic agent used to treat pancreatic, non-small cell lung, and biliary cancer
- 55% - 85% of patients are inherently resistant to gemcitabine or acquire resistance; inherent or acquired resistance caused by
  - Increase in CDA enzyme activity breaking down gemcitabine but is less important for PCS3117
  - Deficiency in hENT1 decreases gemcitabine and PCS3117 transport through the cell membrane
  - Down-regulation of rate-limiting dCK enzyme decreases the formation of cancer-killing nucleotides but does not affect PCS3117 which is activated by UCK2 enzyme



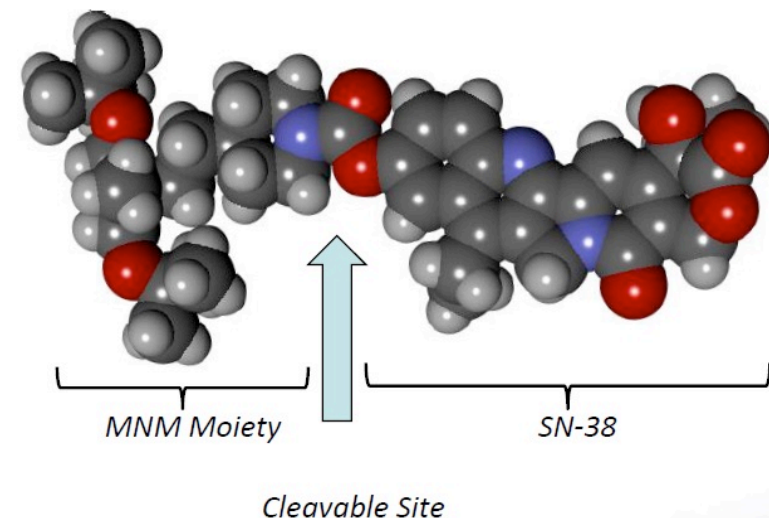
## 2022 Milestones – PCS3117

### Development and Regulatory

- Developing biomarkers to determine if high probability responders to 3117 can be defined prior to treatment so that 3117 can be used following a Precision Medicine approach to therapy; initial assay development to be completed mid-2022
- Although 3117 already has FDA Orphan Designation for the treatment of pancreatic cancer, drug development “roadmaps” are being defined for
  - 2<sup>nd</sup> or 3<sup>rd</sup> line therapy in metastatic pancreatic cancer,
  - 1<sup>st</sup> line therapy for recurrent pancreatic cancer after surgery with Adjuvant Chemotherapy of FOLFIRINOX (folinic acid, fluorouracil, irinotecan, and oxaliplatin), and
  - 1<sup>st</sup> or 2<sup>nd</sup> line therapy in the treatment of biliary tract cancer

# PCS11T: Lipophilic Prodrug of SN-38 (Irinotecan Active Metabolite)

- Pro-drug of SN-38 linking SN-38 to a molecular nano-motor (MNM), a proprietary compound, which interacts with cell membranes preferentially accumulating in the membrane of tumor cells and the tumor core more than normal cells
- Creates an albumin/drug complex (similar conceptually to the albumin-paclitaxel complex in Abraxane) that extends the half-life of SN-38 by 5x compared to irinotecan in pre-clinical studies and likely decrease the side effects
- Given the MNM-SN38 specificity for cancer cells, upon approval it is unlikely that PCS11T will have the BlackBox diarrhea warning which irinotecan has
- Irinotecan sales prior to generics was > \$1B



## Development and Regulatory

- Drug Substance manufacturing site has been selected and Drug Product manufacturing sites are being evaluated
- Drug development “roadmaps” are being developed for lung, pancreatic, colorectal and other potential cancers

# Our People Lead to Success

## Management Team

### **David Young, PharmD. PhD**

Chief Executive Officer, Chairman of the Board

### **Sian Bigora, PharmD.**

Chief Development Officer

### **Michael Floyd**

Chief Operating Officer

### **Patrick Lin**

Chief Business – Strategy Officer

### **James Stanker, CPA**

Chief Financial Officer

### **Wendy Guy**

Chief Administrative Officer

## Board of Directors

### **David Young, PharmD. PhD**

Chairman of the Board, CEO

### **Justin Yorke**

Independent Director  
Manager of the San Gabriel Fund, JMW Fund and the Richland Fund

### **Virgil Thompson**

Independent Director  
Former Chairman of the Board, Questcor Pharmaceuticals

### **Geraldine Pannu**

Independent Director  
Founding and Managing Partner of GLTJ Pioneer Capital

### **Khalid Islam, PhD**

Director  
Former CEO of Gentium  
Chairman of the Board of Fennec Pharm.



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## **Pipeline Background Slides**





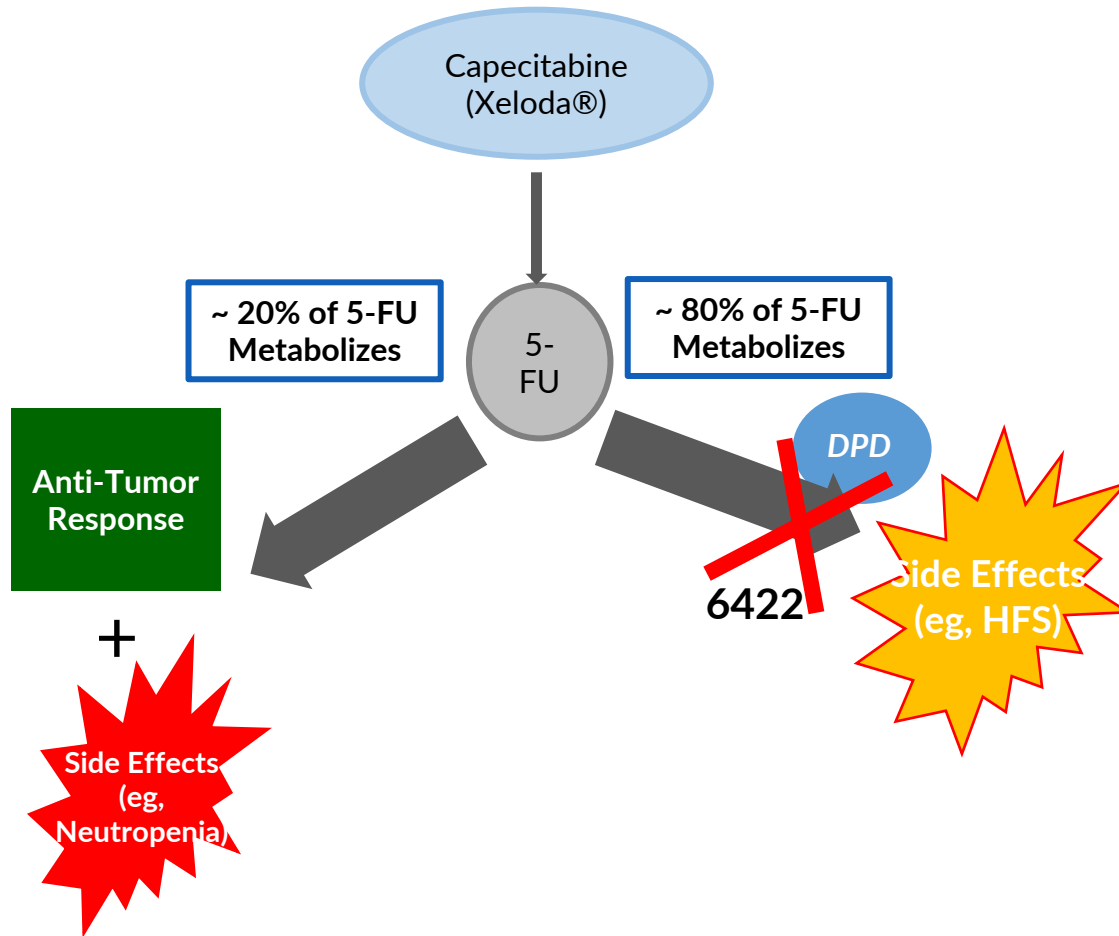
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**Next Generation Capecitabine  
(Combination of Capecitabine with PCS6422)**

**Metastatic Colorectal Cancer, Breast Cancer,  
Pancreatic Cancer**

# Next Generation Capecitabine To Improve Safety/Efficacy Profile (PCS6422 Administered with Capecitabine)

## PCS6422 Irreversibly Inhibits Dihydropyrimidine Dehydrogenase (DPD) Enzyme



### 6422 Inhibits DPD Allowing Two Ways to Win

- **Lower Side Effects** by Lowering 5-FU Metabolite FBAL– Potentially Improve QOL & Reduce Treatment Discontinuations
- **Improve Capecitabine Efficacy** – Potentially Increase Response Rate by Increasing Tumor Exposure to Cancer Killing 5-FU Metabolites

### Economic Value: Initial Markets

- 6422 + Capecitabine combination potentially 1<sup>st</sup> line therapy for a number of cancers (e.g., metastatic colorectal and breast cancer)
- Colorectal cancer; > 145,000 new patients/yr U.S., > 1.8 M total colorectal cancer patients worldwide; > 45% of the new patients with colorectal cancer presently receive capecitabine
- U.S. market potential in colorectal cancer is ~ \$1.0 B

# Next Generation Capecitabine Different than Capecitabine

✓ Response Rate

✓ Survival Time

✓ HFS Rate &/or Severity

✓ % Treatment Resist. Pts

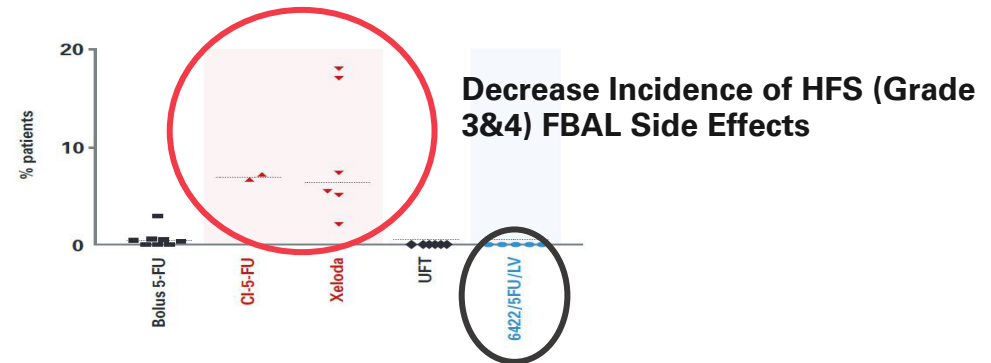
## ➤ Economic Value of Initial Markets

- 6422 + Capecitabine combination potential 1<sup>st</sup> line therapy for a number of cancers (e.g., metastatic colorectal and breast cancer)
- Colorectal cancer; > 145,000 new patients/yr U.S., > 1.8 M total colorectal cancer patients worldwide; U.S. market potential in colorectal cancer is \$700 M - \$1.5 B
- Breast cancer; > 275,000 new patients/yr U.S., > 2.0 M total patients with breast cancer worldwide
- > 45% of the new patients with colorectal cancer presently receive capecitabine
- Potential for Next Generation Capecitabine combination to replace capecitabine in the treatment of colorectal cancer and other cancers

# Unmet Medical Need and Evidence of Clinical Benefit

## ➤ Safety Differentiation of 6422+Capecitabine vs Existing Chemotherapy

- 50-70% of capecitabine patients have adverse events from FBAL resulting in decreasing capecitabine dose or stopping therapy
- Clinical trial of the 6422 + capecitabine provides preliminary evidence that the combination will decrease FBAL adverse events



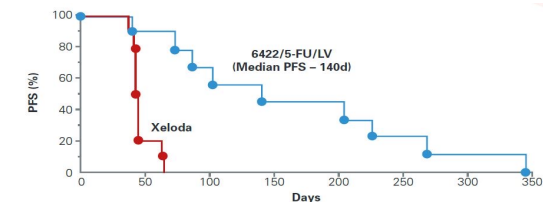
Revollo et al. 2008 Clin Cancer Res; Masuda et al. 2017. NEJM

## ➤ Efficacy Differentiation of 6422+Capecitabine vs Existing Cancer Chemotherapy

- ~30% of patients do not respond at all to capecitabine and ~30% are partial responders
- Clinical trial of the 6422 + capecitabine combination provides preliminary evidence that the combination may extend progression free survival (PFS) in patients who do not respond to capecitabine as well as increase PFS in those patients who do respond

### Improve Capecitabine Efficacy with 6422:

Lower Dose of 6422 Administered Hours Before 5-FU/LV in Capecitabine Resistant Patients



5-FU = 5-Fluoruracil; LV = Leucovorin;  
PFS = Progression Free Survival, SD = Stable Disease; PR = Partial Response; PD = Progressive Disease



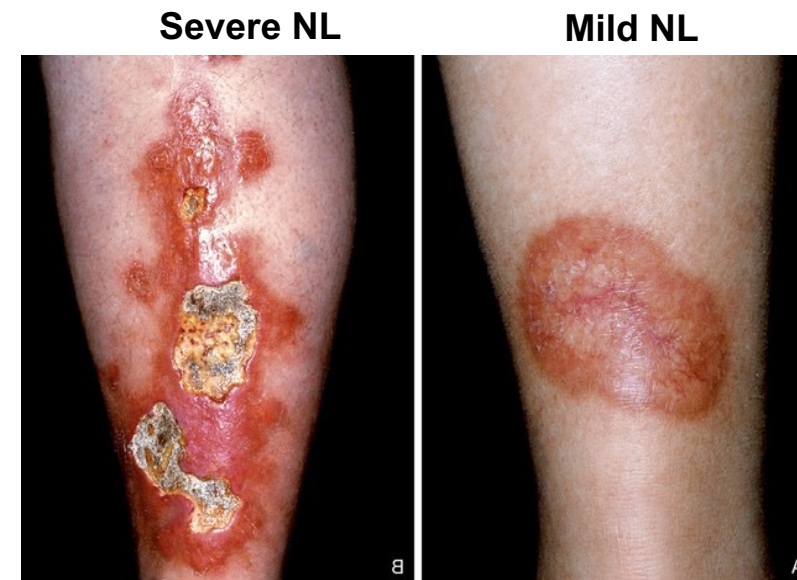
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**PCS499**

**Ulcerative Necrobiosis Lipoidica**

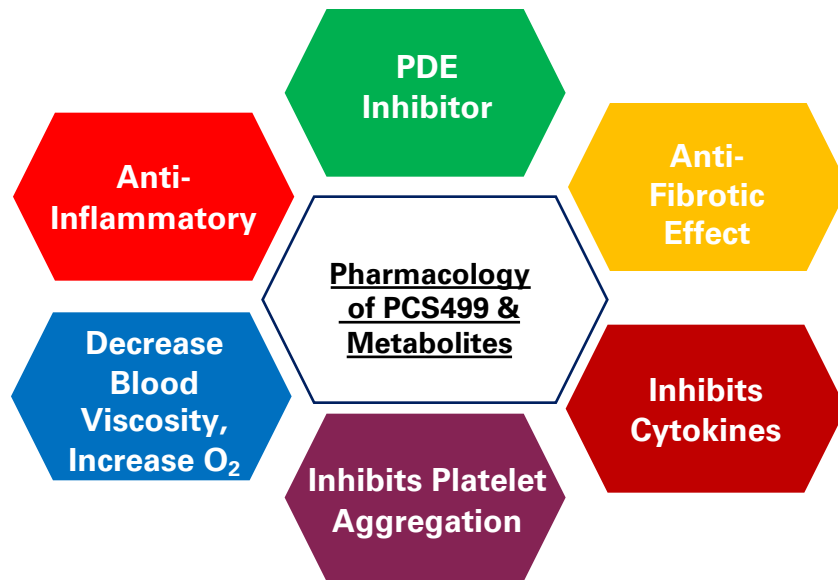
# PCS499 to Be First to Market for the Treatment of Ulcerative Necrobiosis Lipoidica (uNL) or any Form of NL

- Skin, tissue below the skin becomes necrotic, last from months to years with complications such as infections, amputation; Histopathology  $\neq$  diabetic ulcers
- Literature reports 30% of NL patients to have painful ulcers occurring naturally or from contact trauma resulting in approximately 22,000 – 55,000 uNL patients in the U.S with uNL (numbers may actually be significantly less)
- Natural complete healing of moderate to severe ulcers in less than 5% of these patients during the first 1-2 years after onset
- No FDA approved treatment for uNL or NL, no standard of care, all treatments are inadequate
- Market potential of > \$1B even if the prevalence of uNL is significantly less given the unmet medical need in a serious condition



# Unmet Medical Need, Evidence of Clinical Efficacy

- Drugs have been used off-label with mixed success (e.g., pentoxifylline (PTX)); provide poor safety profile given their limited efficacy
- PCS499 is the deuterated analog of a major metabolite of PTX; has identical metabolites and pharmacological targets but PK of 499 + metabolites is different than PTX + metabolites resulting in a better 499 safety profile and allowing the administration of a higher, more efficacious dose of 499



## Pathophysiological Changes in NL

- Decrease in blood flow & Oxygenation
- Decrease in platelet survival
- Increase inflammation
- Increase fibrosis
- Increase cytokines
- Degeneration collagen
- Alters fat deposition

# Unmet Medical Need, Evidence of Clinical Efficacy, PCS499 Improves Benefit-Risk

- PCS499 is the deuterated analog of a major metabolite of PTX; has identical metabolites and pharmacological targets but PK of 499 + metabolites is different than PTX + metabolites resulting in a better 499 safety profile and allowing the administration of a higher, more efficacious dose of 499
- 499 + metabolites target pharmacology that directly affect 6 of the 7 NL pathophysiological changes
- 1.8 gm/d of 499 has a better safety profile than 1.2 gm of PTX in animal tox studies and Phase 1 healthy human volunteer studies
- In the Phase 2A study of 10 NL and 2 ulcerative NL patients, all ulcers closed in the 2 ulcerative NL patients, including new contact trauma ulcers, and 1.8 gm/d was well tolerated







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**PCS12852**

**Gastroparesis**

# 2H'22 - PCS12852 Trial Conduct Completed

## PCS12852 Potent and Selective 5HT<sub>4</sub> Agonist for Treatment of Gastroparesis

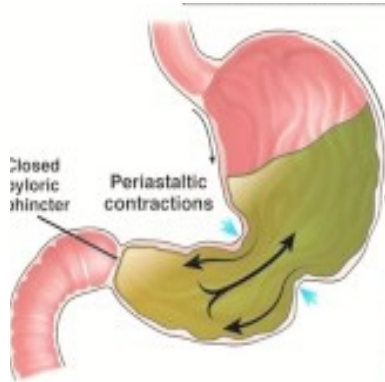
### ➤ Target Indication:

- Treatment of moderate to severe gastroparesis

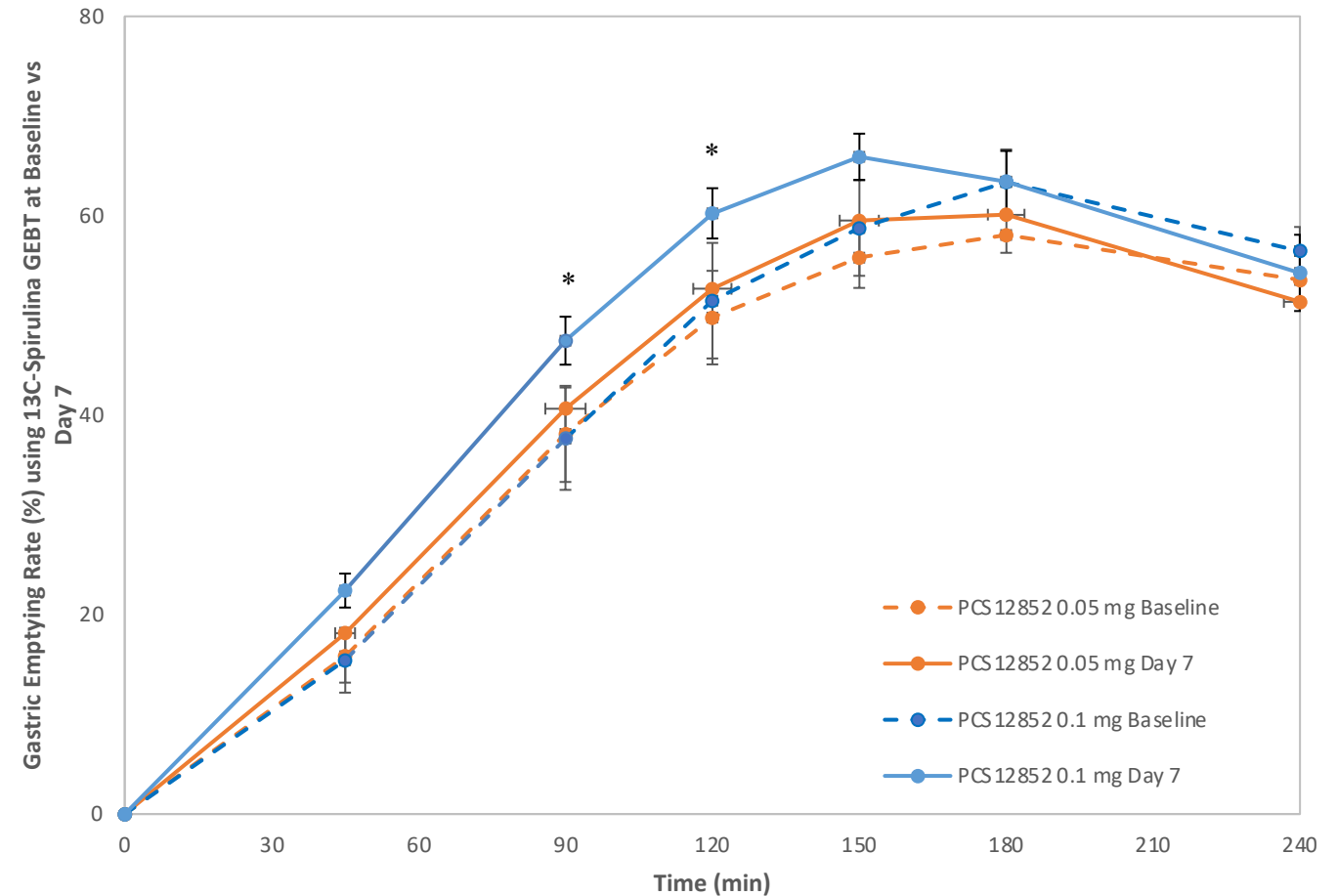
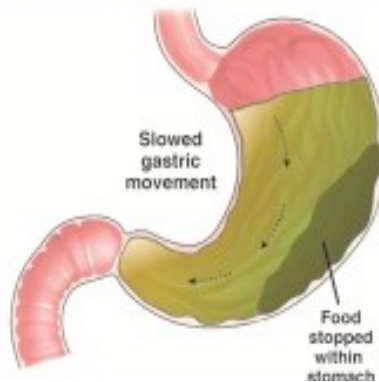
### ➤ Target Claims:

- Improves gastric emptying rate and the symptoms associated with moderate to severe gastroparesis (e.g., bloating, pain, nausea, vomiting)

Normal Gastric Emptying



Gastroparesis



# PCS12852: Potent & Selective 5HT4 Agonist for Treatment of Gastroparesis (\$1.5B Market)

	PCS12852	Other 5HT4 Drug (e.g., Cisapride, Prucalopride, Mosapride)	Dopamine D2 Antagonist (e.g., Metoclopramide)
Target Population	<ul style="list-style-type: none"> <li>Potentially all gastroparesis patients (e.g., diabetic, idiopathic)</li> </ul>	<ul style="list-style-type: none"> <li>Diabetic gastroparesis patients</li> </ul>	<ul style="list-style-type: none"> <li>Diabetic gastroparesis patients</li> </ul>
Binding	<ul style="list-style-type: none"> <li>Specific &amp; potent 5HT4 receptor binding</li> </ul>	<ul style="list-style-type: none"> <li>Less specific binding to 5HT4 than 12852</li> <li>Less potent than 12852</li> </ul>	<ul style="list-style-type: none"> <li>Binds to Dopamine D2 receptors</li> </ul>
Side Effects	<ul style="list-style-type: none"> <li>No serious side effects in clinical studies to date</li> </ul>	<ul style="list-style-type: none"> <li>Serious cardiovascular side effects (e.g., cisapride removed from market)</li> <li>Suicidal ideation (e.g., prucalopride)</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning serious neurological side effects, Side effects require limited use</li> </ul>
Efficacy	<ul style="list-style-type: none"> <li>Increase gastric emptying rate in patients with constipation</li> </ul>	<ul style="list-style-type: none"> <li>Increase gastric emptying rate</li> <li>Successful treatment demonstrated</li> </ul>	<ul style="list-style-type: none"> <li>Only drug FDA approved for treatment of gastroparesis</li> </ul>

- Existing FDA approved drugs and off-labeled prescribed drugs are mainly used for the treatment of diabetic gastroparesis
- All these drugs have a poor side effect profile limiting their use
- Present market size for gastroparesis is estimated to be over \$1.5B
- Phase 2A is a placebo-controlled, randomized, dose-response trial evaluating gastric emptying rate and symptom relief in gastroparesis patients
- Primary endpoints in Phase 2B and Phase 3 trials will be based on symptoms

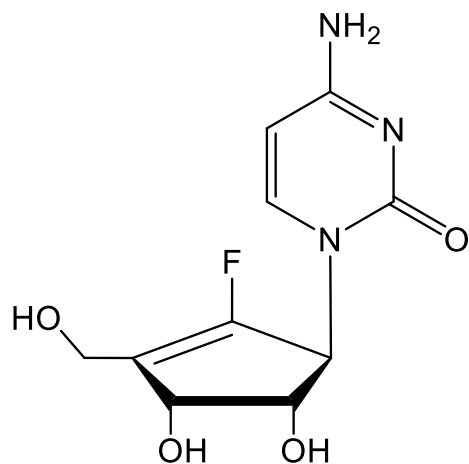


Processa Pharmaceuticals

**PCS3117**

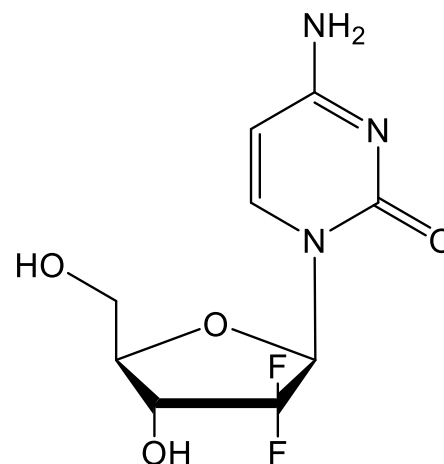
**Metastatic Pancreatic Cancer, Biliary Cancer,  
Other Cancers**

# 1H'22 - PCS3117 Biomarker Assay Development Completed



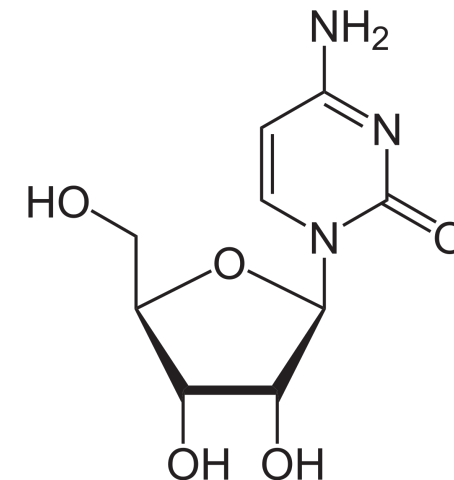
RX-3117

Oral Administration  
(Cytosine + Ribose Analog)



Gemcitabine (dFdC)

IV Administration  
(Cytosine + F,F-Deoxyribose)



Cytidine

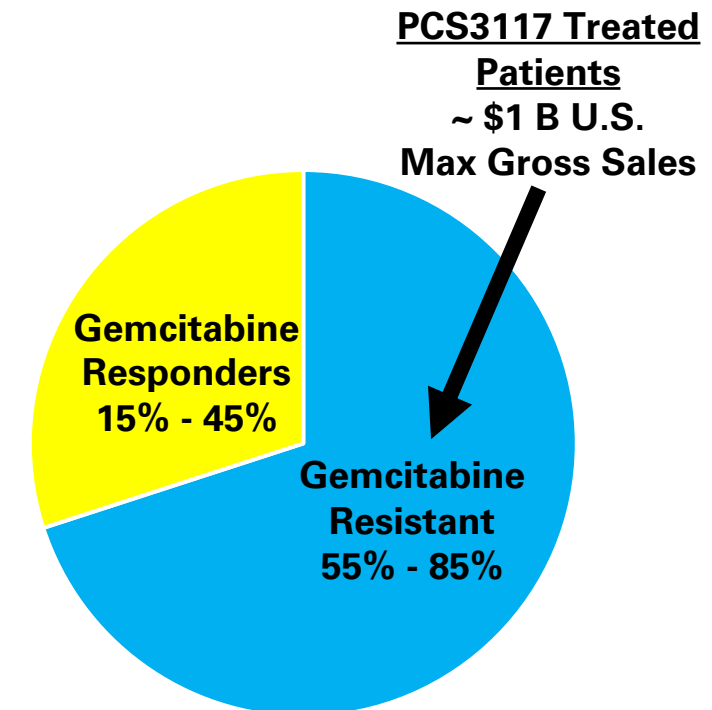
(Cytosine + Ribose Ring)

## ➤ Gemcitabine Market

- First-line treatment for locally advanced or metastatic pancreatic cancer; inoperable, locally advanced or metastatic non-small cell lung
- Second-line and third-line treatment for ovarian cancer and other types of cancer
- Gross Sales: \$815 M U.S., \$1.7 B worldwide

# PCS3117 for Cancer Patients Resistant to Gemcitabine

- PCS3117 has a similar structure to gemcitabine but is activated through a different pathway and causes cancer cell apoptosis in more ways than gemcitabine
- PCS3117 has been shown in gemcitabine resistant cancer patients and tumor animal models to alter cancer progression
- Gemcitabine is the most widely used chemotherapeutic agent used to treat pancreatic, non-small cell lung, and biliary cancer
- 55% - 85% of patients are inherently resistant to gemcitabine or acquire resistance; inherent or acquired resistance caused by
  - Increase in CDA enzyme activity breaking down gemcitabine but is less important for PCS3117
  - Deficiency in hENT1 decreases gemcitabine and PCS3117 transport through the cell membrane
  - Down-regulation of rate-limiting dCK enzyme decreases the formation of cancer-killing nucleotides but does not affect PCS3117 which is activated by UCK2 enzyme



# PCS3117 Prior Evidence of Clinical Efficacy and Safety in Cancer Patients

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- PCS3117 monotherapy Phase 2A trial as second or third-line therapy in patients with progressive metastatic pancreatic cancer after 1-5 previous therapies of chemotherapy (93% (40/43) refractory to gemcitabine)
  - 31 % (14 patients) had progression-free survival (PFS) for 2 months
  - 12% (5 patients) had stable disease for more than 4 months
  - One patient had a tumor reduction of 40% after 28 days of treatment
  - A previous report of gemcitabine as 2nd line therapy had only 17% disease-free progression
  - Mild to moderate adverse events reported with a better overall safety profile than gemcitabine
- PCS3117 + Abraxane Phase 2A trial as first-line therapy in chemotherapy naïve patients with metastatic pancreatic cancer
  - Overall response rate of 23% observed in patients (9/40)
  - Median progression-free survival of 5.4 months
  - Overall response rate was better than previous reports with only Abraxane
  - Overall response rate was no better than previous reports with gemcitabine + Abraxane



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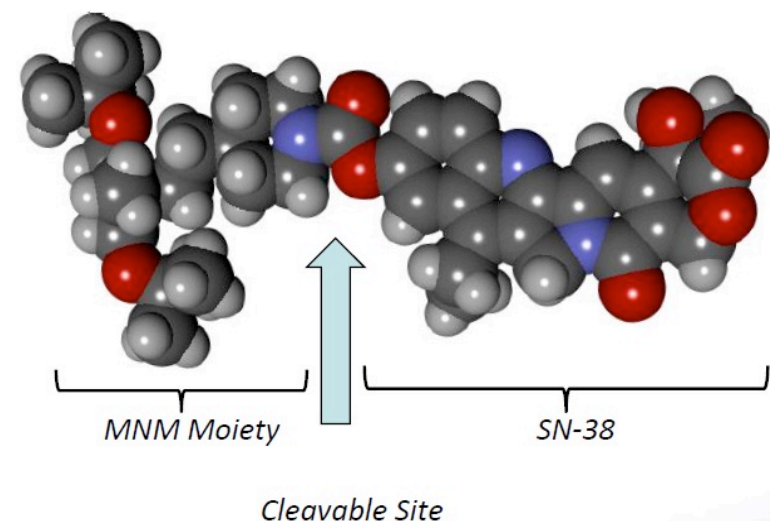
**PCS11T**

**Small Cell Lung, Pancreatic, Colorectal, Other  
Cancers**



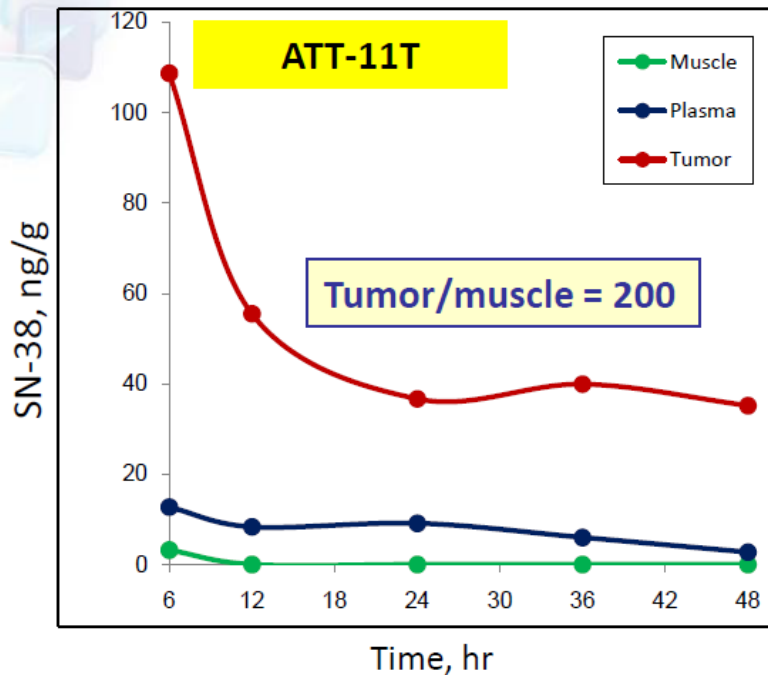
# PCS11T: Lipophilic Prodrug of SN-38 (Irinotecan Active Metabolite)

- Pro-drug of SN-38 linking SN-38 to a molecular nano-motor (MNM), a proprietary compound, which interacts with cell membranes preferentially accumulating in the membrane of tumor cells and the tumor core more than normal cells
- Creates an albumin/drug complex (similar conceptually to the albumin-paclitaxel complex in Abraxane) that extends the half-life of SN-38 by 5x compared to irinotecan in pre-clinical studies and likely decrease the side effects
- Given the MNM-SN38 specificity for cancer cells, upon approval it is unlikely that PCS11T will have the BlackBox diarrhea warning which irinotecan has
- Irinotecan sales prior to generics was > \$1B
- Drug Substance manufacturing site has been selected and Drug Product manufacturing sites are being evaluated
- Drug development “roadmaps” are being developed for lung, pancreatic, colorectal and other potential cancers

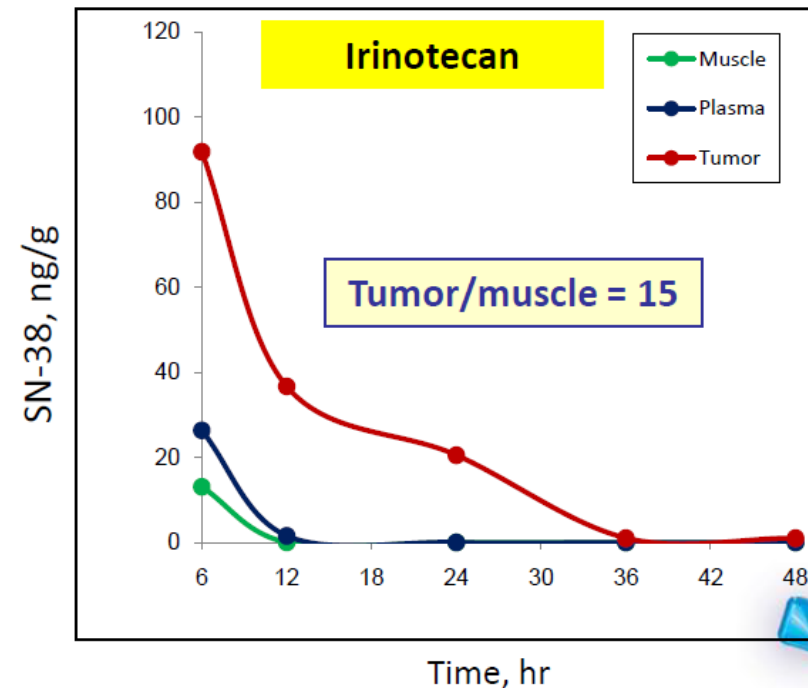


# Higher and More Selective Tumor Exposure to SN38 with PCS11T (formerly ATT-11T) versus Irinotecan

Tumor-bearing mice had 200x higher drug in tumor vs muscle compared to 15x with Irinotecan



Tissue	AUC, ng/g*hr	Tumor/ organ ratio
Tumor	3,855	1
Plasma	403	9.57
Muscle	19.2	200



Tissue	AUC, ng/g*hr	Tumor/ Organ ratio
Tumor	1,153	1
Plasma	172	6.70
Muscle	78	15

# Efficacy Maintained at Lower Doses of PCS11T When Compared to Irinotecan in SW620 Colorectal Cancer Xenograft Model

