



Combined Company Investor Presentation

June 2022

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This presentation includes information about investigational agents. The efficacy and safety of such investigational agents have not yet been established. Drug development is uncertain and investigative agents may be terminated along the development process.

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Combined Company Presents A Unique Opportunity: Multi-Targeted Approach to Reset Dysregulated Biology

Scientific focus on polyamines, key regulators of normal biology altered in many disease states

- 1
 - Our drug targeting strategies may allow for product opportunities in therapeutic areas of high unmet medical need, including oncology and orphan diseases
- 2
 - Combined pipeline spans from pre-clinical to Phase III registration programs
 - Late-stage programs are orphan oncology related: pancreatic cancer and FAP (familial adenomatous polyposis)
- 3
 - Approximately a \$5 Billion aggregate market potential across lead indications
- 4
 - Commercial partner for Phase III FAP program: fully funded registration program in the US
 - Company retains ROW rights
- 5
 - Strategic synergies and partnerships (NCI, SWOG, COG, JDRF)

Combining clinical development programs to create significant shareholder value

Highly Experienced Management Team with Proven Track Record

Proven orphan and oncology drug discovery, development and commercialization expertise



Dr. Jennifer Simpson
Chief Executive Officer

15+ Years



Sue Horvath
Chief Financial Officer

15+ Years



Dr. Thomas Neenan
Chief Scientific Officer

22+ Years



Rachel Bragg
VP, Clinical Development

14+ Years



Dr. Elizabeth Bruckheimer
VP, Drug Dev & Reg Affairs

13+ Years

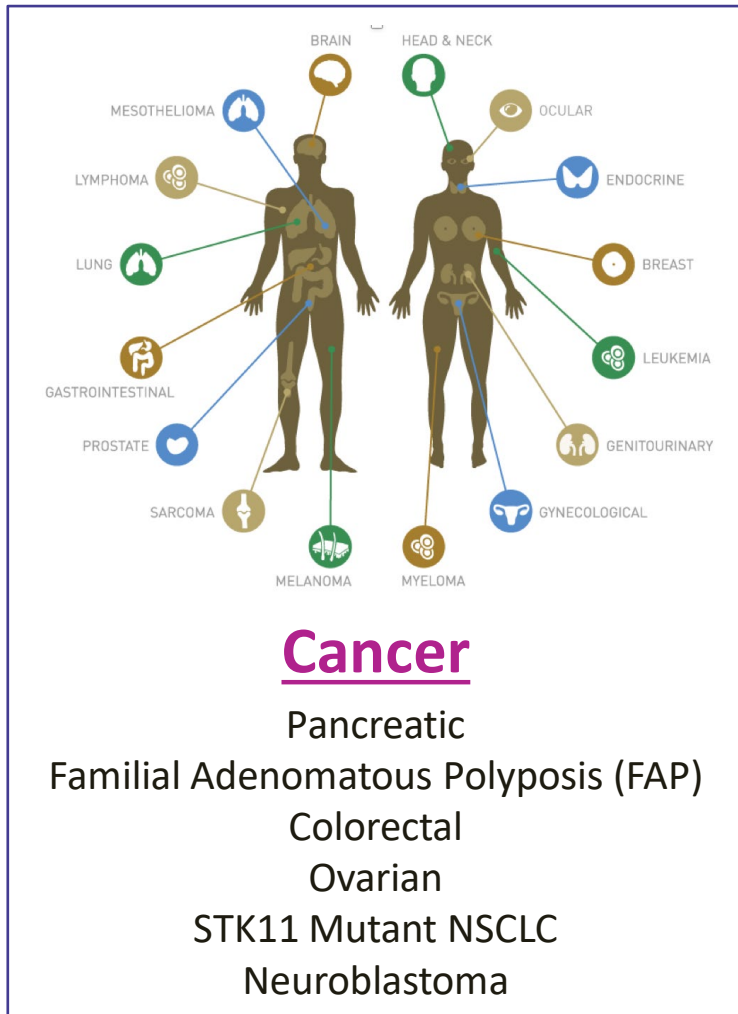


Dr. Ashok Chavan
VP, CMC, QA, Supply Chain

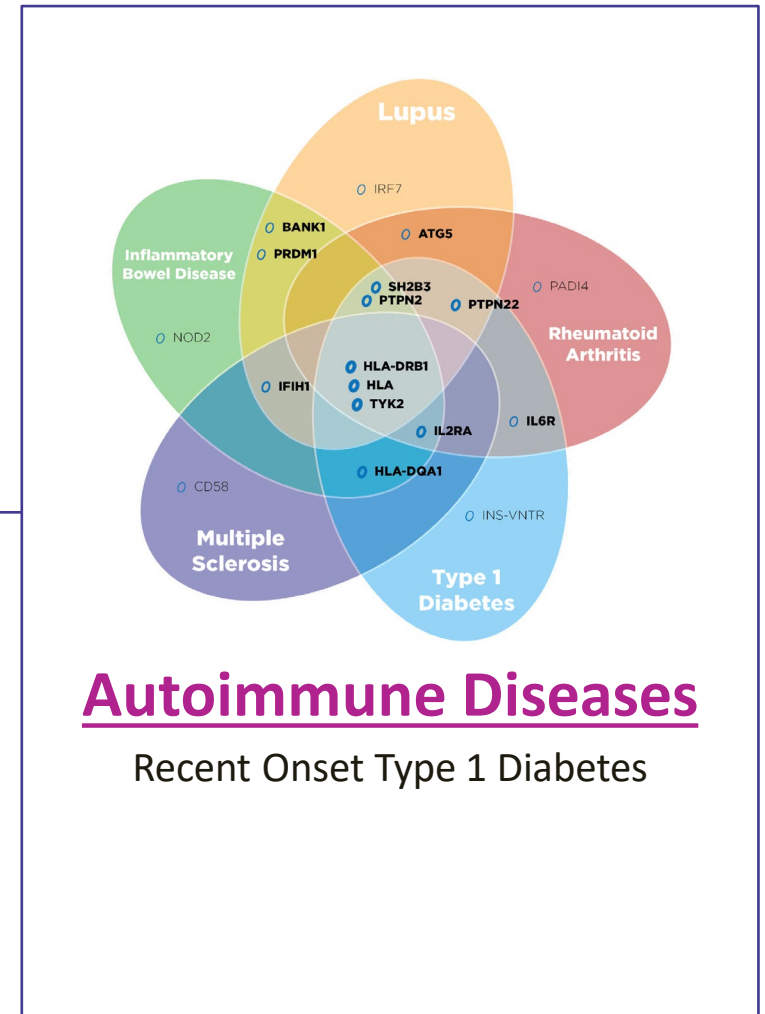
15+ Years

CombinedCo Team collectively has 10+ FDA approvals and decades of Pharma experience positioning Panbela to execute on the clinical development programs

Dysregulation of the Polyamine Pathway Leads to Disease



Polyamine Dysregulation in Disease

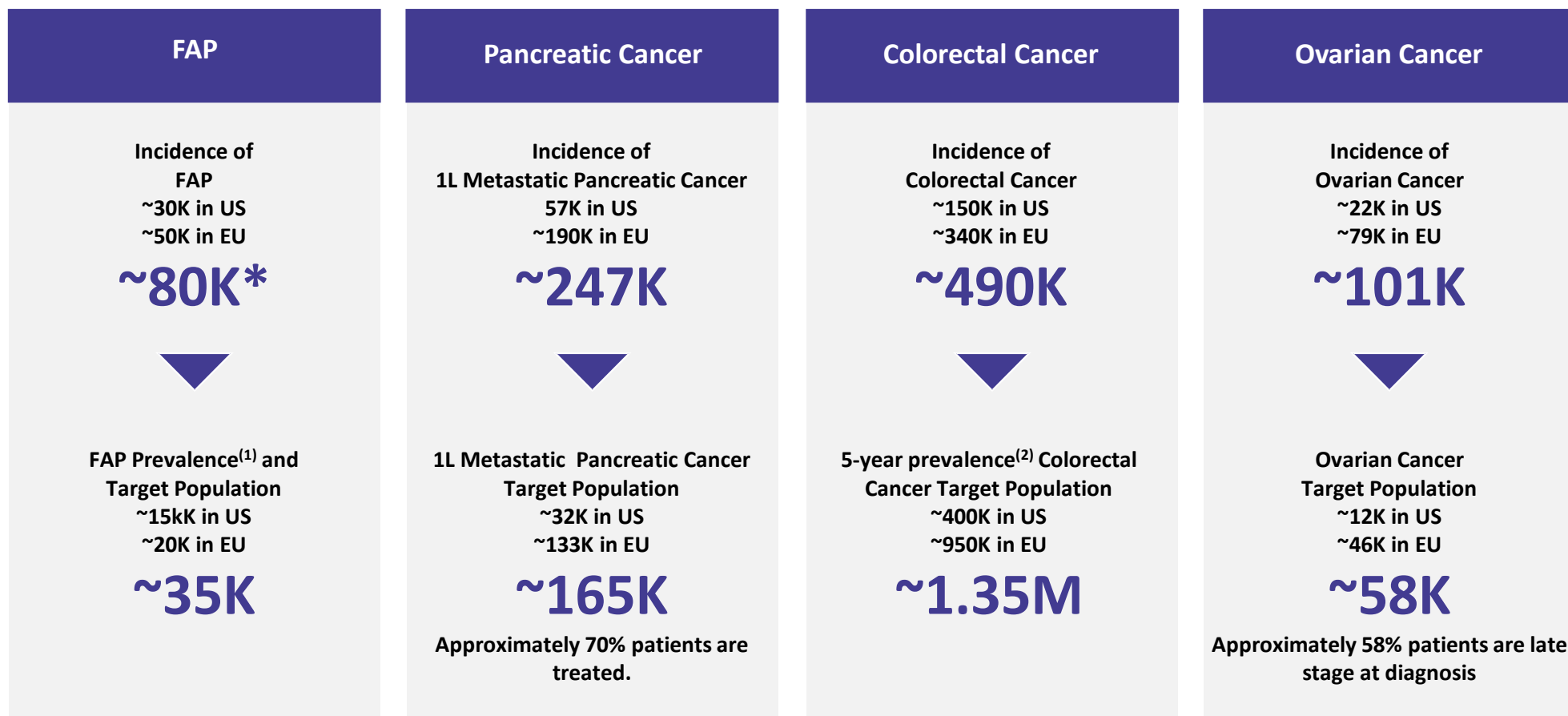


Initial focus on oncology and autoimmune disease - enhancing anti-tumor activity, preventing tumor growth, and modulating the immune system

Combined Pipeline May Address Unmet Needs

	Preclinical	IND Ready	Phase I	Phase II	Phase III	Milestones
Flynpovi (eflornithine/ sulindac combination tablet)	Familial Adenomatous Polyposis (FAP) (Partnered in US; CPP Pursuing EU/Asia Approval)					<ul style="list-style-type: none">➤ Fully funded by licensing partner➤ FPI – 1H 2023
	Colon Cancer Risk Reduction (NCI Fund via Partnership with SWOG)					<ul style="list-style-type: none">➤ Futility Analysis – End of 2022
SBP-101 (injection)	PDA (First Line Metastatic)					<ul style="list-style-type: none">➤ Phase II/III Ongoing; Interim Analysis Q1 2024
	PDA Neoadjuvant					<ul style="list-style-type: none">➤ Phase II Ready – Open 2H 2022
	Ovarian					<ul style="list-style-type: none">➤ Phase I Ready – Open Mid 2022
CPP-1X-S Immunotherapy Enhancement (eflornithine sachets)	Relapsed Refractory Neuroblastoma (Chemo + Unituxin) with COG/NCI					<ul style="list-style-type: none">➤ Phase I Ready FPI – 2H 2022➤ Phase II FPI – 2H 2023
	NSCLC (STK11 Mut) with Keytruda					
	PD1 Inhibitor-nonresponsive Cancers					
CPP-1X-T (eflornithine 250 mg tablets)						<ul style="list-style-type: none">➤ Phase II Ready FPI 2H 2022➤ Indiana University / JDRF / Panbela Collaboration Announcement – 2H 2022
	Early Onset Type 1 Diabetes					<ul style="list-style-type: none">➤ Publication of Phase I Results – End of 2022/Q1 2023

Potential Market Opportunity for Lead Programs



FAP Source: Burt et al 2010; Varesco et al 2004; multiple KOL sources.

Pancreatic Cancer Source: American Cancer Society. Cancer Facts & Figures 2021. Atlanta, GA: American Cancer Society; 2021 and European Cancer Information Systems data 2020 (<https://ecis.jrc.ec.europa.eu/>).

Colorectal Cancer Source: NCI Seer statistics 2018 and <https://ecis.jrc.ec.europa.eu/>, https://seer.cancer.gov/csr/1975_2018/browse_csr.php?sectionSEL=1&pageSEL=sect_01_table.21 and GLOBOCAN 2020.

Ovarian Cancer Source: American Cancer Society. Cancer Facts & Figures 2021. Atlanta, GA: American Cancer Society; 2021 and European Cancer Information Systems data 2020 (<https://ecis.jrc.ec.europa.eu/>).

1) Based on 1/10,000 prevalence, excludes 5% with no APC mut. Includes ages 15-74 and only patients with intact colon or retained rectum (~70% of FAP patients).

2) Prevalence is for "1st invasive tumor ever".

Complementary Pharmacotherapies Targeting Dysregulation

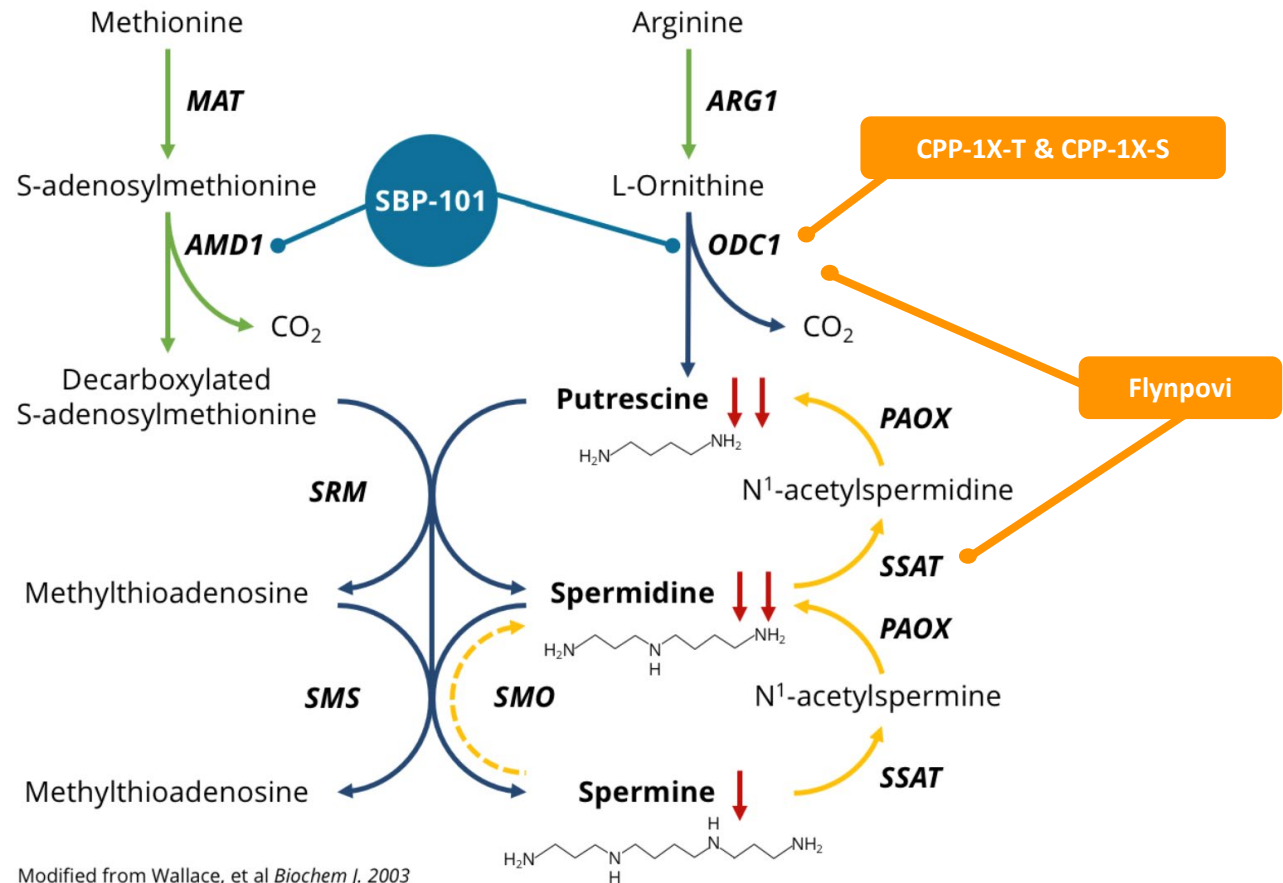
Pipeline Objective

The objective of Panbela's pipeline is the utilization of pharmacotherapies to reduce/normalize increased disease-associated polyamines using complementary pharmacotherapies

Current Pipeline

- 1 SBP-101
- 2 Flynpovi
- 3 CPP-1X-T
- 4 CPP-1X-S

Combined pipeline pharmacotherapies hit different targets in the polyamine pathway





FLYNPOVI: A combination of CPP-1X and Sulindac

Lead Product Opportunity – CPP-1X and Sulindac (Flynpovi)

Familial Adenomatous Polyposis (FAP)

- A genetic disease caused by APC mutations where colon polyps develop early in life
- Nearly 100% of patients will develop colon cancer if the polyps are left untreated

Prevalence

1-in-10,000

~30K in US

~50K in EU

Global Markets Opportunity

Key Information:

- No approved FAP drugs on the market
- Target Physicians: Gastroenterologists
- US-only potential revenue at market share of 35%-60% (approximately 11,300-18,400 potential patients)

Pricing:

Annual Price	US only Potential Annual Revenue
\$20,000	\$227M - \$368M
\$25,000	\$284M - \$460M
\$30,000	\$341M - \$552M
\$35,000	\$397M - \$644M

North American Royalties from Licensee:

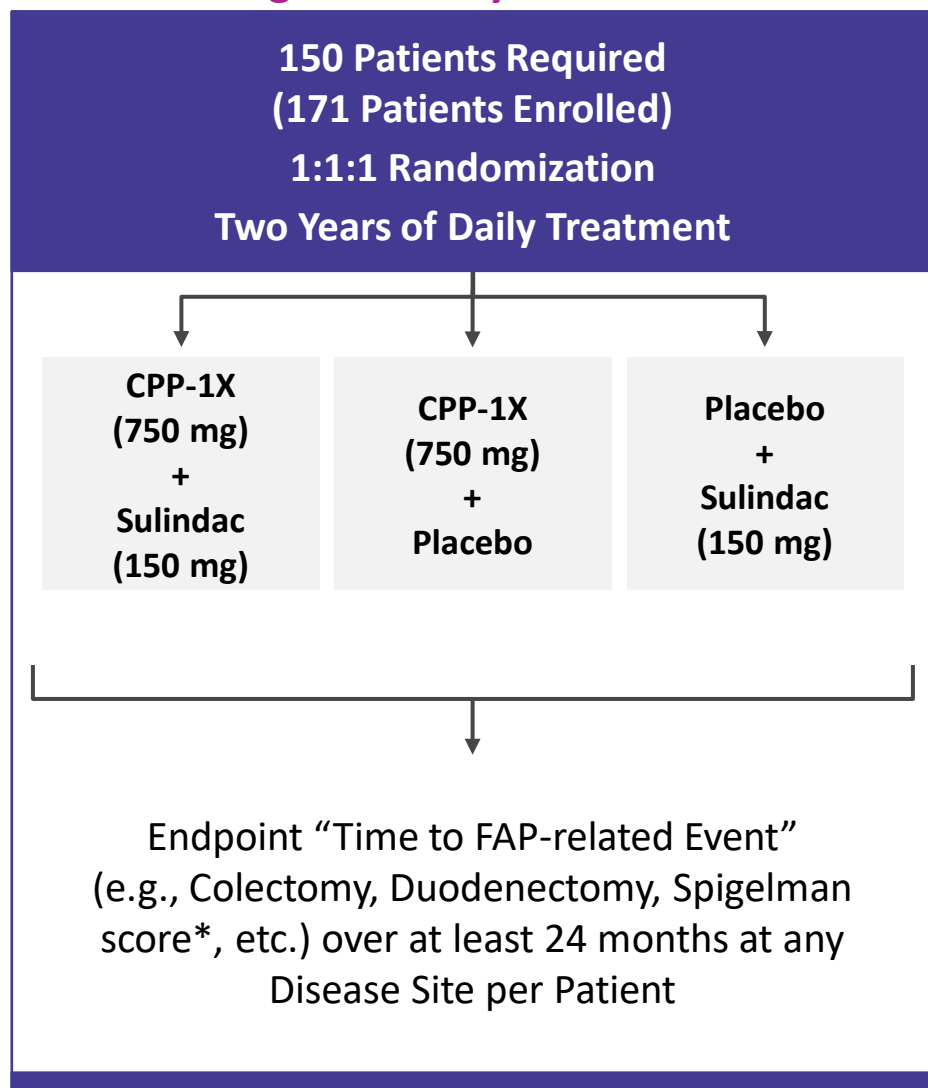
- Capped: 25% up to \$100 million in total payments
- Uncapped: 5% after capped royalty is reached

Market:

- FAP affects all ethnicities
- In addition to the US - Significant market opportunity in Europe, China and Japan

FAP-310 Trial: “Time to Delay FAP-related Event” Endpoint

CPP FAP 310 global study



Time to delay FAP-related events

Composite Endpoint including surgeries, polyp removal, and upper GI scoring system (“Spigelman”)*; based on FDA/EMA recommendation-first ever “event” trial in FAP

Surgical endpoints most meaningful

p value with all elements of composite endpoint = 0.28 (i.e., with unvalidated non-surgery scoring system* included)

$p = <0.02$ in delaying surgical and interventional events in “lower GI”

* Determined to not be a “clinically meaningful” metric resulting in a change in the clinical management or treatment for the patient

Burke et al 2021 NEJM

Balaguer et al 2021 DCR

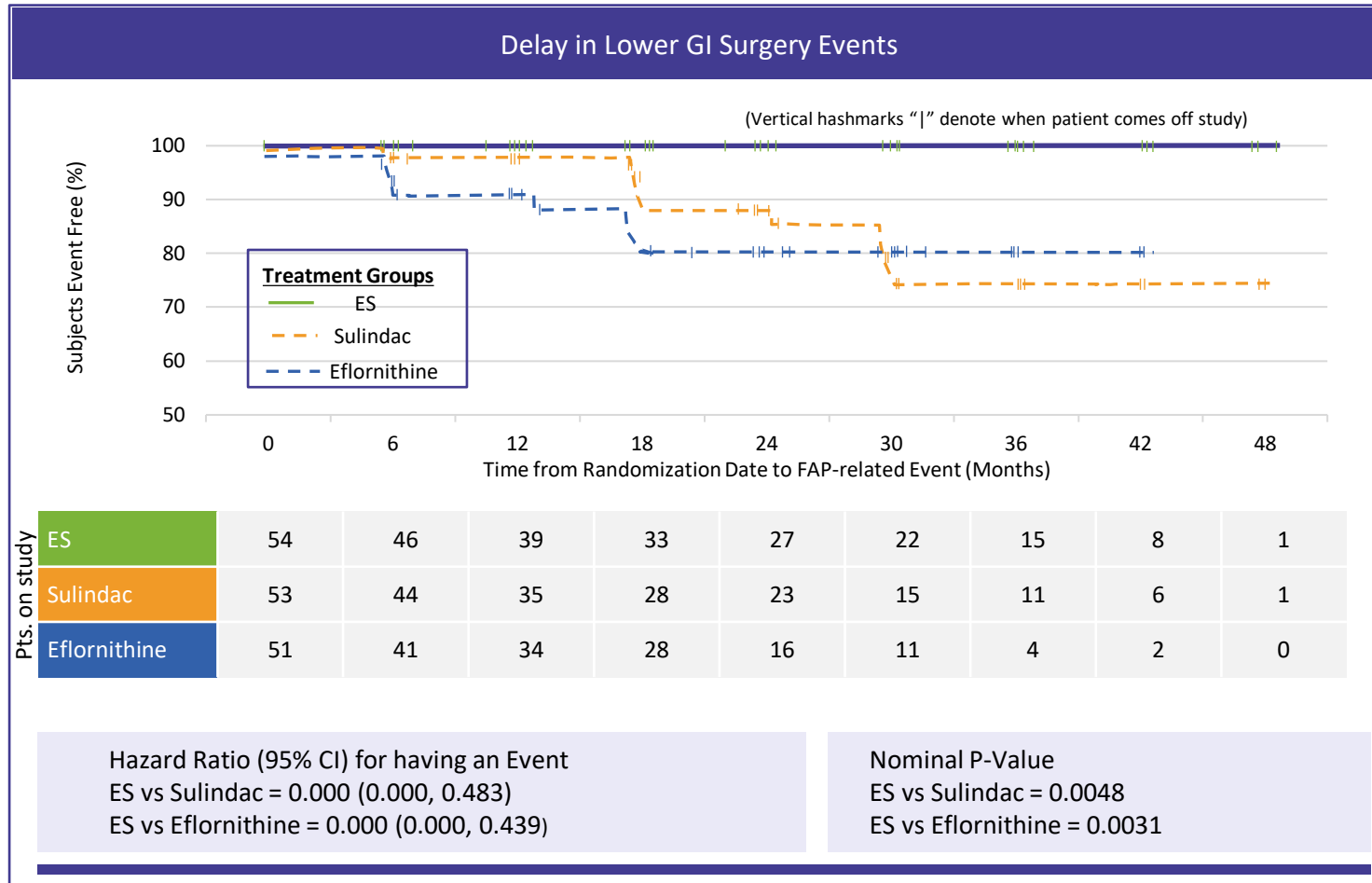
No Lower GI Surgeries for Flynpovi Combination

Event Rate Distribution of FAP-Related Surgery Events in Lower GI

Surgery Events	ES Combo	Eflornithine	Sulindac	Overall
	(N=56)	(N=57)	(N=58)	(N=171)
Need colectomy	0	3	4	7
Need proctectomy	0	1	1	2
Need pouch resection	0	4	1	5
Total Surgical Events	0	8	6	14
Event Rate	0/56 (0%)	8/57 (14%)	6/58 (10%)	14/171 (8%)

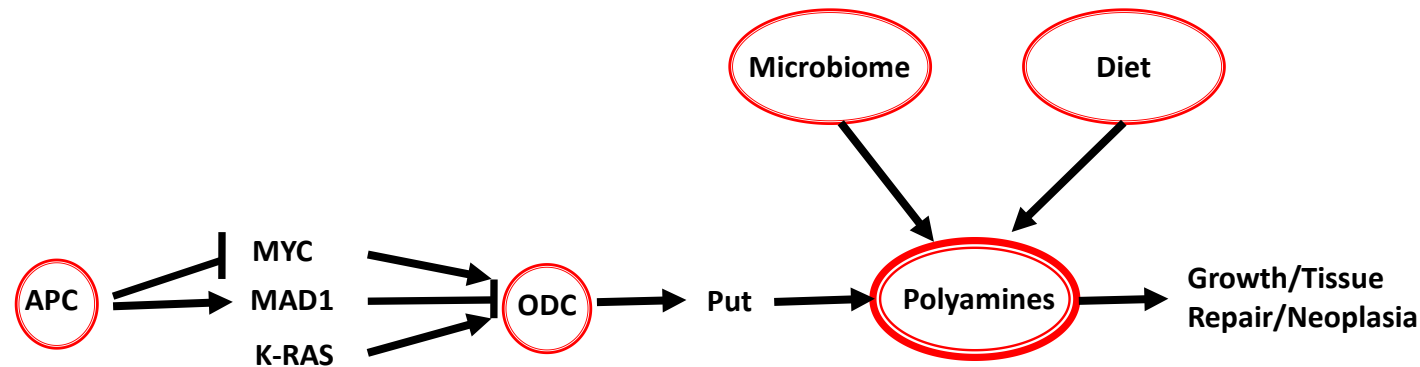
No surgeries in Lower GI in ES Combo arm

Flynpovi Combination Delays Need for Lower GI Surgery



In Subjects with Lower GI Anatomy (i.e., excludes 13 patients with ileostomy)

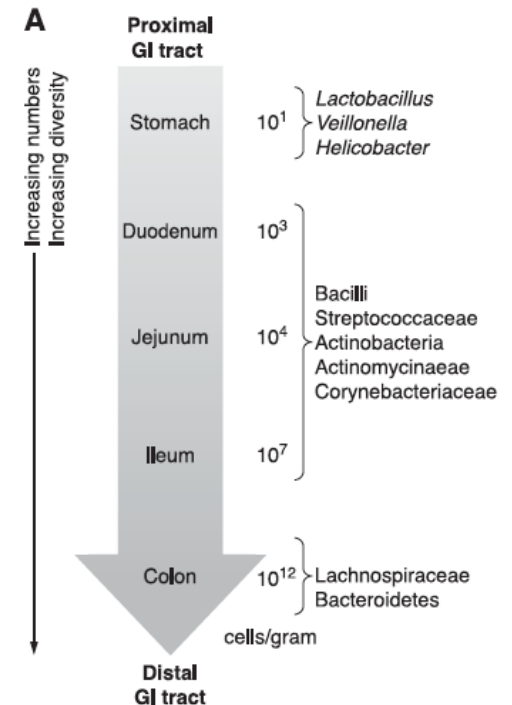
Rationale for Efficacy of Flynpovi in the Lower Gastrointestinal Tract of FAP Patients



- Polyamines drive uncontrolled growth, polyposis, and cancer.
- Polyamines can be synthesized but also derived from the diet and microbiome.
- The mechanism of disease driven by polyamines which are upregulated in gastrointestinal mucosa in FAP patients - **Eflornithine target, ODC is increased 2.5-fold with APC mutation**
- The colon has 9 orders of magnitude more microbiome than upper GI that contribute to polyamines levels.
- **Flynpovi acts by a dual mechanism of action suppressing de novo synthesis and increasing the export of polyamines. The overall goal is to prevent or delay the onset of cancer through the regression or prevention of colonic adenomas through the reductions in polyamines.**

High Concentrations of the Microbiota Contribute to the Impact of Polyamines in The LGI

- ▶ The microbiota increases steadily along the gastrointestinal tract.
 - **Small numbers in the stomach but very high concentrations in the colon.**
 - **Areas of the LGI contain up to nine orders of magnitude (10^9) more bacteria than that in the duodenum and other areas of the UGI.**
- ▶ Microbiota produces **biofilms which increase polyamines leading to colonic epithelial cell proliferation and colorectal cancer development**
- ▶ Colonic mucosa of FAP patients can harbour biofilms containing tumorigenic bacteria
- ▶ **Microbiota provides a potential mechanism of action for the enhanced efficacy of Flynpovi in the LGI via polyamines.**



Adverse Events of Special Interest

Adverse Events of Special Interest	Flynpovi (Eflornithine + Sulindac Combination) N=56 Subjects (%)	Sulindac N=57 Subjects (%)	Eflornithine N=56 Subjects (%)
Anemia	1 (1.8)	5 (8.8)	2 (3.6)
Myelosuppression	0	1 (1.8)	0
Thrombocytopenia	0	3 (5.3)	1 (1.8)
Cardiovascular/Thrombotic events	1 (1.8)	1 (1.8)	1 (1.8)
Hearing impairment/Tinnitus	5 (8.9)	8 (14.0)	2 (3.6)
Non-bleeding GI event	33 (58.9)	25 (43.9)	28 (50.0)
Bleeding GI event	17 (30.4)	17 (29.8)	10 (17.9)
Headache/Migraine/Tension Headache	8 (14.3)	13 (22.8)	7 (12.5)
Dizziness/Vertigo	4 (7.1)	4 (7.0)	7 (12.5)

- **Comparable safety** amongst all treatment arms

Basis for FDA Complete Response Letter

■ Clinical

- Single pivotal study efficacy was based on exploratory post-hoc analysis using a modified primary endpoint in a subgroup of the intent-to treat population
 - Asked to perform a new study focused on FAP patients with an intact lower-GI tract which showed statistically significant effect in post-hoc analysis of FAP-310 trial

■ Quality

- Proposed dissolution condition for testing of Eflornithine is different from the FDA Guidance for Industry: Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products
 - ✓ Revised dissolution specifications
- Limited discriminating ability of the dissolution method for compression force and no discriminating ability for the magnesium stearate or sulindac particle size distribution
 - Dissolution method being revised to address concerns

Moving Ahead: New Phase III Trial

Moving Ahead 2022

- **North America Licensee funding next trial**
- **FDA and EMA focus on new Phase III trial :**
 - Lower GI focus (LGI), informed by positive data from FAP-310 and regulatory feedback
 - Reaffirm current clarity & acceptable aspects of CMC, clin pharm, and non-clinical package
 - Initiate new LGI focused pivotal trial
- **FDA:**
 - Type A meeting in US for new trial (via Licensee): 2H22
 - Initiate new trial: 1H23
- **EMA:**
 - Select National Competent Authority (NCA) engagement on new trial and clear registration path (Sweden/Netherlands based on CHMP feedback)
 - Follow up SAWP engagement with revised approached, informed by CHMP and NCA interactions

Summary of Approach to Approval

Strong Results in the Lower GI

- ✓ Focus on Lower GI: statistically significant p-values and hazard ratios for clinically meaningful surgical endpoints—emphasized by regulators—in Phase III pivotal trial
- ✓ Expected safety profile over 2-4 years of daily dosing in Phase III pivotal trial
- ✓ Totality of the evidence includes mechanistic, preclinical, and clinical supportive data

No Other Approved Therapy for this Orphan Disease



SBP-101

Preliminary Efficacy of SBP-101 + Gemcitabine/Nab-paclitaxel in First-Line Metastatic Pancreatic Ductal Adenocarcinoma

	BEST OVERALL RESPONSE				Overall Response	Disease Control
	CR	PR	SD	PD		
SBP-101 (0.40 mg/kg) + G/A* (Ph1a COHORT 2) n=7	0	5 (71%)	2 (29%)	0	5/7 (71%)	5/7 (71%)
SBP-101 (0.40 mg/kg) + G/A* (Ph1a COHORT 4 + Ph1b) n=29	1 (3%)	13 (45%)	10 (34%)	5 (17%)	14/29 (48%)	24/29 (83%)
Gemcitabine + Nab-paclitaxel (G/A*)** n=431	<1%	23%	27%	20%	23%	48%

	PFS			OS		
	Ph1a 2	Ph1a 4+Ph1b	G+A*	Ph1a 2	Ph1a 4+Ph1b	G+A*
SBP-101 (0.40 mg/kg) + G/A Cohort						
Median (mo)	5.6	6.5	5.5	10.3	14.6***	8.5
6 mo (%)	43	54	44	100%	86%	67%
12 mo (%)	0	18	16	43%	55%	35%

*G/A = gemcitabine + Nab-paclitaxel

**Historical control data, MPACT study G+A arm, N=431 - Source: Von Hoff NEJM 2013

*** Final Data-3/18/22

Ph1a = Phase Ia

Ph1b = Phase Ib

CR-Complete Response; PR-Partial Response; SD-Stable Disease

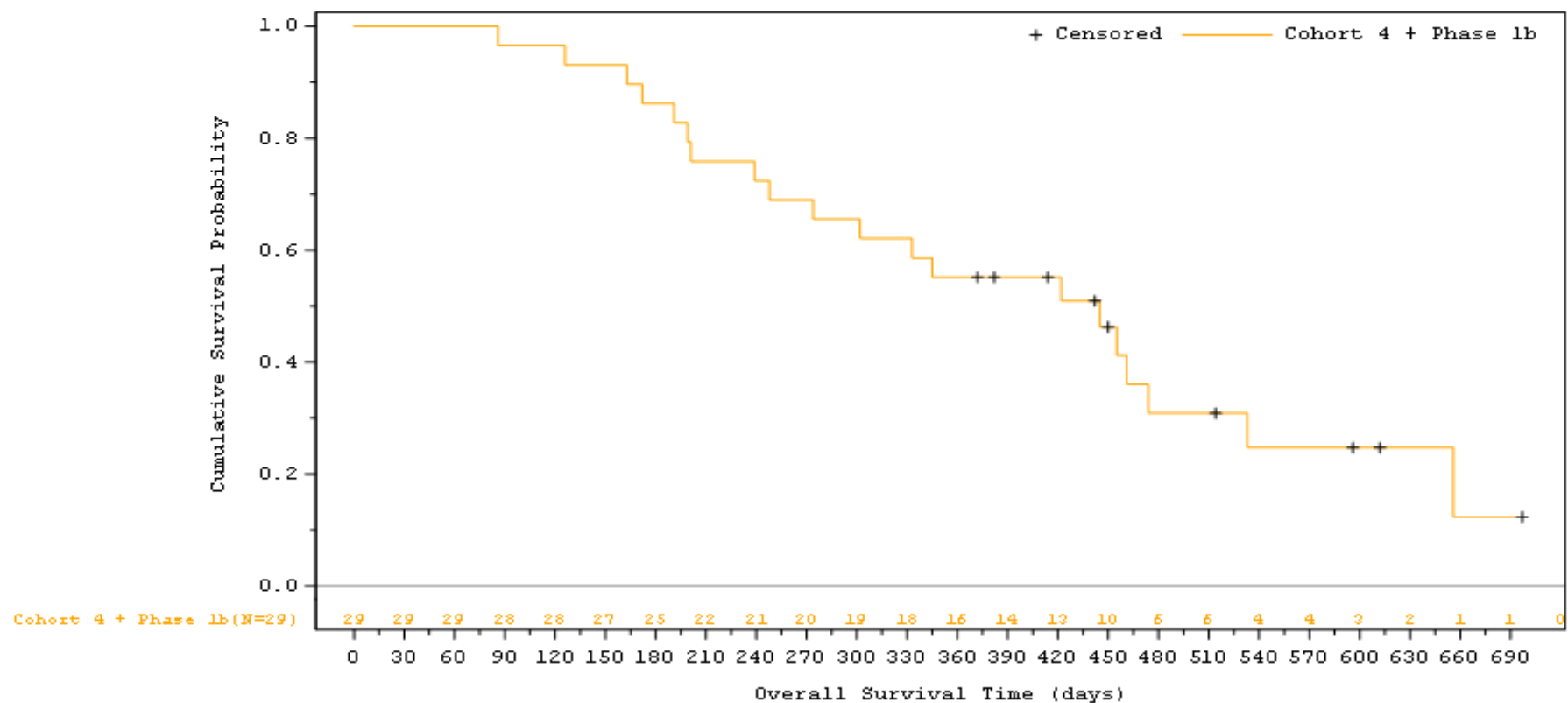
Disease Control Rate = CR+PR+SD for > 16 weeks

Efficacy Comparison

Treatment	OS	PFS	ORR	DCR	PD
CL-SBP-101-03 ¹	14.6 months	6.5 months	48.3%	82.8%	4.8%
FOLFIRINOX ²	11.1 months	6.4 months	31.6%	70.2%	15.2%
Modified FOLFIRINOX ³	10.2 months	6.1 months	35.1%	86.5%	13.5%
Gemcitabine + Abraxane – Phase 1/2 ⁴	12.2 months	7.9 months	48%	68%	16%
Gemcitabine + Abraxane (MPACT) ⁵	8.5 months	5.5 months	23%	48%	20%

1. CL-SBP-101-03 CSR (modified Efficacy Evaluable data n=29);
2. Conroy et al, 2011;
3. Stein et al, 2016 (MPC data);
4. Von Hoff et al, 2011;
5. Von Hoff et al, 2013

SBP-101 + Gemcitabine/Nab-paclitaxel Overall Survival*



Cohort 2 N=7: 2 patients with long term survival.

- One still alive at 33.1 months
- One deceased at 30.3 months

Cohort 4+1b = 6 patients still alive

SBP-101 + Gemcitabine/Nab-paclitaxel Demonstrated a Similar Safety Profile to Gemcitabine/Nab-paclitaxel in First-Line Metastatic Pancreatic Ductal Adenocarcinoma

Safety Results

Grade ≥3 AEs of Special Interest	N	SBP-101%		G+A %**
Hematologic Events				
Neutropenia	20	40%		38%
Leukopenia	0	-		31%
Anemia	9	18%		13%
Thrombocytopenia	1	2%		17%
Febrile Neutropenia	1	2%		3%
Non-hematologic Events				
Diarrhea	7	14%		6%
Fatigue	6	12%		17%
Peripheral Neuropathy	3	6%		17%

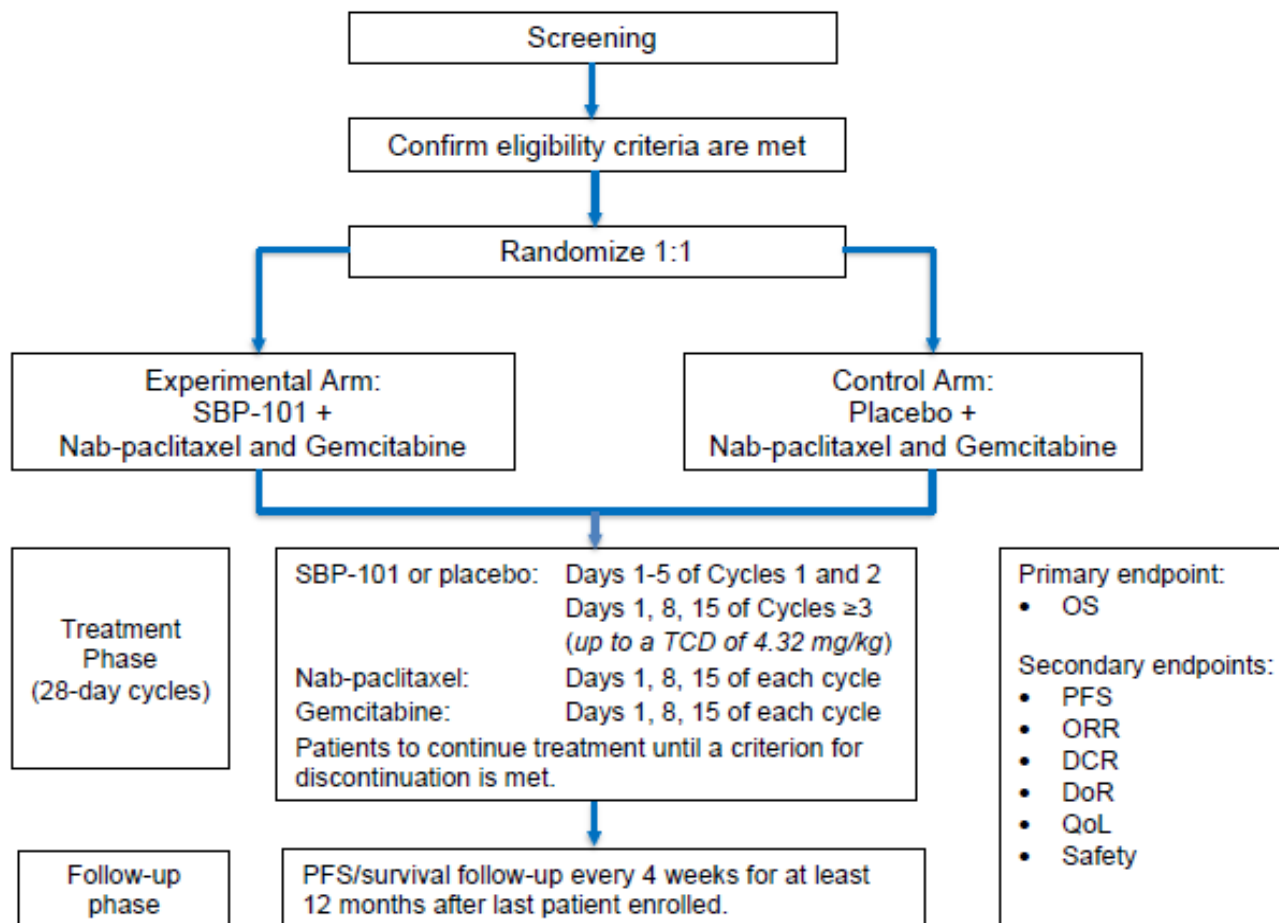
Grade ≥3 adverse events attributable to any study medication, N=50.				
Event	SBP-101	G+A**	All 3	Total N (%)
Neutropenia	0	19 (1G, 18 G+A)	1	20 (40%)
Elevated LFTs	5	0	9	14 (28%)
Anemia	0	7 (G+A)	0	9 (18%)
Diarrhea	0	6 (4A, 2G+A)	1	7 (14%)
Fatigue	0	4 (G+A)	2	6 (12%)
Vision events	4	1 (G)	2	7(14%)
Dehydration	2	2 (1A, 1 G+A)	0	4 (8%)
Peripheral neuropathy	0	3 (A)	0	3 (6%)

*Historical control data, MPACT study, G+A arm, N= 431 - Source: Von Hoff 2013

** G/A = gemcitabine + Nab-paclitaxel

Phase II/III Pancreatic Cancer Trial Initiated 1Q 2022 in Subjects Previously Untreated for Metastatic Pancreatic Ductal Adenocarcinoma

A Randomized, Double-Blind, Placebo Controlled Study of Nab-Paclitaxel and Gemcitabine with or Without SBP-101

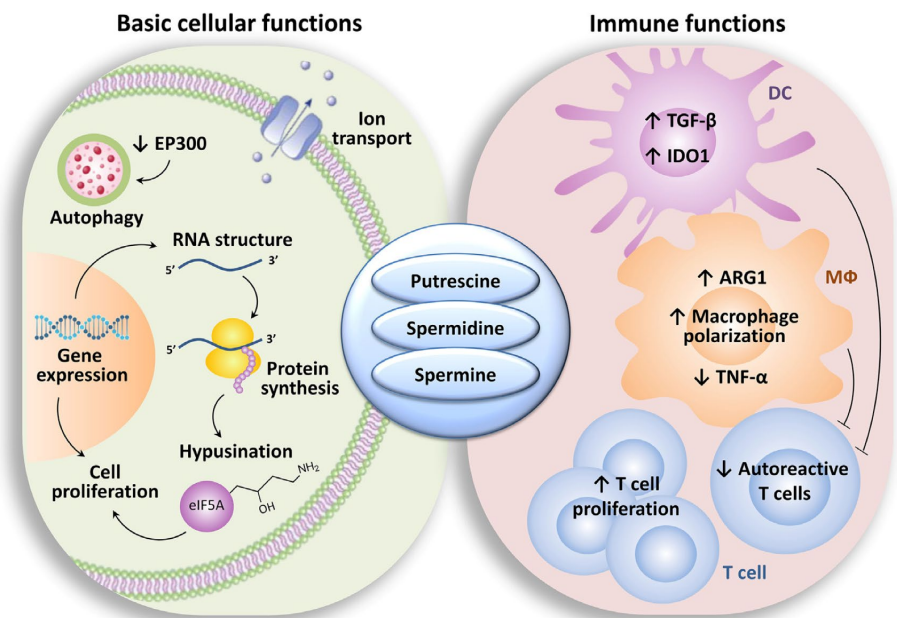




Polyamines & Immune Dysregulation

Role of Polyamines in Immune Dysregulation

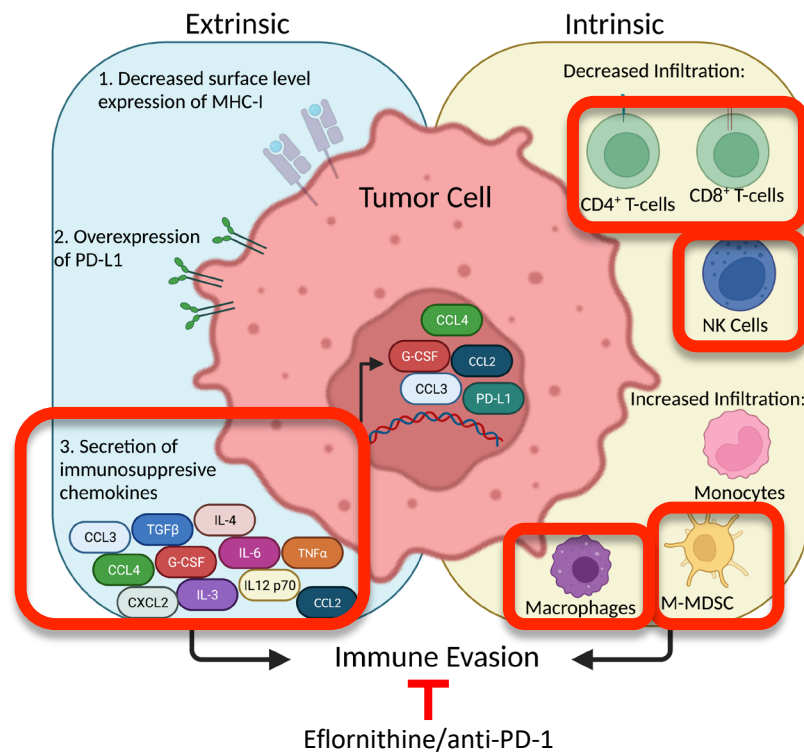
- Immune systems require multiple soluble and cellular components, including polyamines, for a normal immune function
- High levels of polyamines are present in tumor cells and in autoreactive B- and T-cells in autoimmune diseases
- Dysregulation of polyamines can result in:
 - Tumor immune evasion
 - Elevated cell stress
 - Increased autoimmunity
- Panbela's pipeline focuses on **resetting the polyamine pathway to restore normal immune function**



Proietti E et al 2020 Trends in Immunol

Rationale for Eflornithine/anti-PD-1 Combination

- Targeting Ornithine decarboxylase (ODC) using eflornithine unmasks antitumor T cell immune response by weakening of tumor-induced immune suppression that is mediated by Myeloid-Derived Tumor Suppressor Cells (MDSCs).
- The addition of anti-PD-1 prevents the functional exhaustion of these surviving T cells leading to enhanced antitumor effects.
- The combination of eflornithine/anti-PD1 prevents immune evasion
- **Targeting the polyamine pathway, treatment may reinvigorate the T cell-directed activity of an anti-PD-1 therapy and promote immune-mediated elimination of tumor cells.**





CPP-1X-S

Rationale for CPP-1X-S (Eflornithine Sachets) in STK11 Mutant NSCLC

- In preclinical tumor models, eflornithine treatment improves anti-PD-1 efficacy by:
 - Increasing tumor-specific cytotoxic T-cell populations
 - Increasing expression of PD-1 on tumor-associated CD8+ T cells
- ~10% of NSCLC cancers have STK11 mutations
- STK11 mutant NSCLC tumors have:
 - Reduced cytotoxic T-cells infiltrates
 - Upregulation of the arginine pathway which utilizes ODC to increase levels of the polyamine putrescine
 - Respond poorly to immune checkpoint inhibitor therapy

STK11 Mutant NSCLC Investigator-Initiated Trial

*Collaborating with investigators at Moffitt Cancer Center on Phase I/II trial: “**Targeting Ornithine Decarboxylase as an Immunotherapeutic Target in STK11 (LKB1) Pathway-Deficient Non-Small Cell Lung Cancer**”*

Patient Population

- Stage IV NSCLC
- Immune Checkpoint Inhibitor Naïve
- STK11 mutant

Phase I

Standard Pembro +
CPP-1X-S Dose
Escalation (PD-L1 \geq 1%)

Primary Endpoint: Toxicity



Phase II

Standard Pembro + CPP-1X-S
(Dose from Phase I)
(PD-L1 \geq 1%)

Primary Endpoint: Efficacy
(Response Rate)
Secondary Endpoints: Overall Survival,
Progression-free Survival

Currently finalizing **trial protocol**, manufacturing **CPP-1X-S** (eflornithine sachet product), and completing **regulatory requirements**



Business Overview

Summary of Upcoming Milestones

1H 2022

- ASCO GI Poster Presentation – Interim Phase I 1L mPC
- Close Transaction
- FPI – Randomized Phase II/III 1L Metastatic Pancreatic Cancer Trial (mPC)
- Final Data – Phase I 1L mPC
- Initiation of Ovarian Cancer Clinical Program

2H 2022

- FAP Global Registration Trial (sponsored by Licensee), Type A FDA Meeting
- FPI – Phase I STK11 Mutant NSCLC IIT
- Gastric Cancer Prevention Phase II Results
- Initiation of Phase II Neoadjuvant Pancreatic Cancer IIT

Proforma Financial Position and Capital UNAUDITED

Panbela

Cash at 3/31/22	7,386,000
Common Stock at 3/31/22	13,449,117
Shares reserved for Options (WAE = \$5.76)	2,449,531
Shares reserved for Warrants (WAE = 4.59)	5,109,501
Total Outstanding and Reserved	21,008,149

Cancer Prevention Pharmaceuticals (CPP)

Cash at 3/31/22	215,000
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Proforma Combined Company

Common Stock Outstanding held by Current Panbela Shareholders	59%	13,449,117
Common Stock held by Legacy CPP Shareholders (includes Options & Warrants)	41%	9,345,996
Total Common Stock outstanding at Closing		22,795,003
Anticipated Debt after Closing (Sucampo and Tillotts)		6,840,000

Summary: Combination of PBLA and CPP

Unique Scientific Approach: Resetting dysregulation via polyamine pathway



Multiple targets and products in the pipeline



Broad, late-stage pipeline opportunities



Multiple data readouts expected



Experienced management team



Significant market potential