



Investor Presentation April 2023

Last modified April 26, 2023

Panbela Therapeutics

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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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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

- Multiple near term inflection points
- CPP acquisition completed in 2022 to create complementary, multiproduct, multi-indication portfolio
- Late-stage programs are orphan oncology related: pancreatic cancer and FAP (familial adenomatous polyposis)
- Combined pipeline spans from pre-clinical to Phase III registration programs
- 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

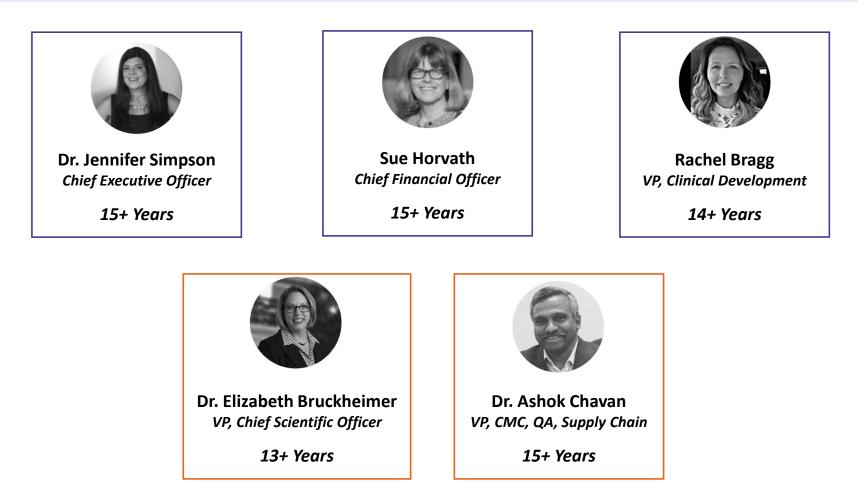
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Strategic synergies and partnerships (NCI, SWOG, COG, JDRF, JHU SOM)

Combined clinical program pipeline to create significant shareholder value

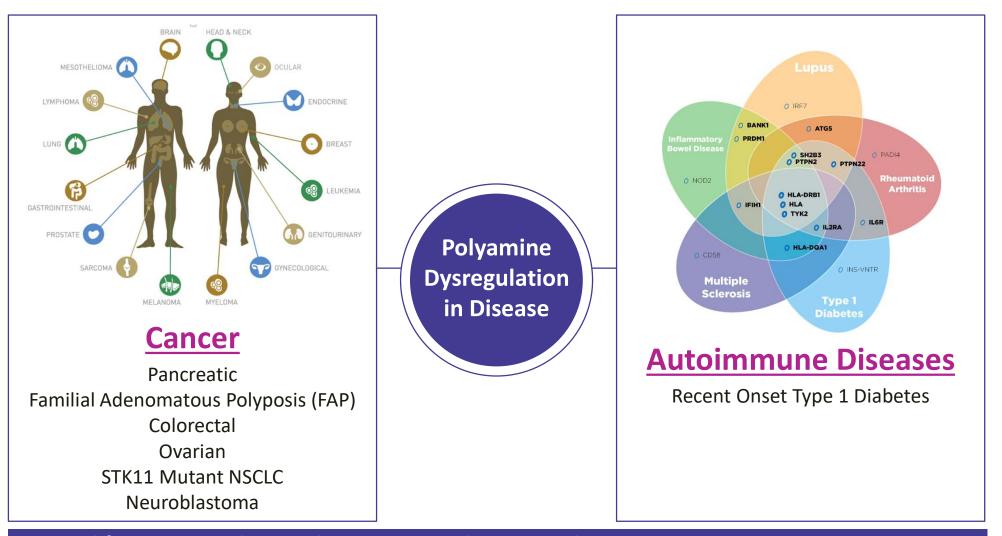
Highly Experienced Management Team with Proven Track Record

Proven orphan and oncology drug discovery, development and commercialization expertise



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



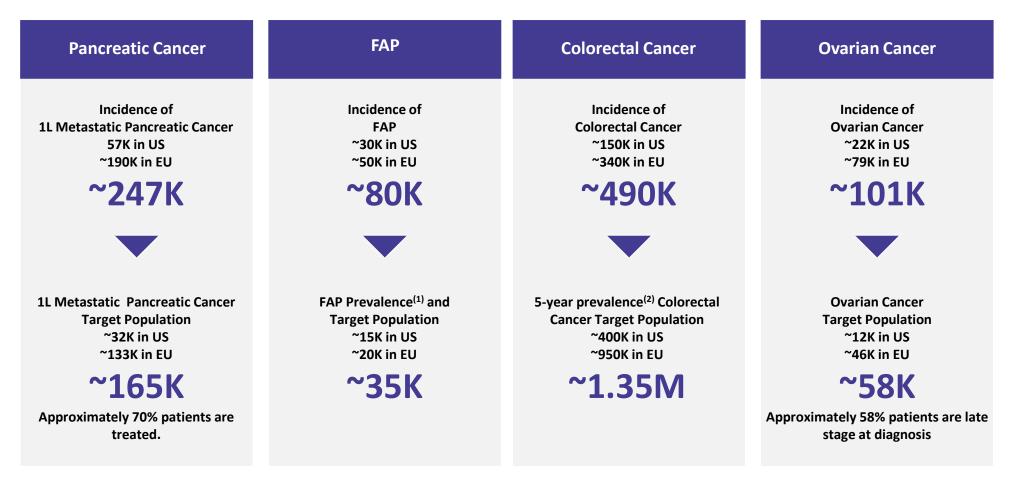
Initial focus on oncology and autoimmune disease - enhancing anti-tumor activity, preventing tumor growth, and modulating the immune system

http://ibeliveit.ca/Personalized-Cancer-Medicine/Funding-byCancer-Typr.aspx https://www.benaroyaresearch.org/blog/post/mystery-multiple-autoimmune-diseases NSCLC- Non Small Cell Lung Cancer

Pipeline May Address Multiple Unmet Needs

	Preclinical	IND Ready	Phase I	Phase II	Phase III	Milestones	
SBP-101 (ivospemin) (Injection)	PDA (First Line Me	Phase III Ongoing; Interim Analysis Q1 2024					
	PDA Neoadjuvant					Phase II Ready – Open 1H 2023	
v <u>3</u> =	Ovarian					Phase I Ready – Open Early 2023	
Flynpovi (eflornithine/ sulindac combination tablet)	Familial Adenomat	tous Polyposis (FAP) (Partnered in US; CPP	Pursuing EU/Asia App	roval)	 Global Harmonization of Registration Protocol by 2H 2023 	
Fly (eflor su combina	Colon Cancer Risk	Reduction (NCI Fund	via Partnership with S	SWOG)		Futility Analysis – 1H 2023	
• S rapy ent achets)	Relapsed Refracto						
CPP-1X-S Immunotherapy Enhancement (eflornithine sachets)	NSCLC (STK11 Mu	t) with Keytruda				 Phase I NSCLC Ready FPI – 1H 2023 Phase II NSCLC FPI – 2H 	
C Imm Ent (eflorn	PD1 Inhibitor-noni		2023				
CPP-1X-T (eflornithine 250 mg tablets)						 Phase II Ready FPI 1H 2023 Indiana University / JDRF / 	
	Early Onset Type 2	1 Diabetes				Panbela Collaboration Announcement – 1H 2023	
						 Publication of Phase I Results – 1H 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/).

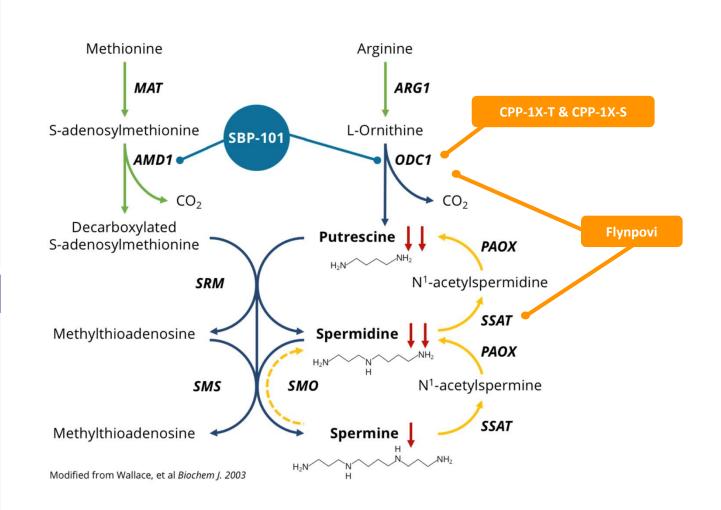
1) Based on 1/10,000 prevalence, excludes 5% with no APC mut. Includes ages 15-74 and only patients with intact colon or retained rectum (~70% of FAP patients). 2) Prevalence is for "1st invasive tumor ever".

Complementary Pharmacotherapies Targeting Dysregulation

Pipeline Objective

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

Combined pipeline pharmacotherapies hit different targets in the polyamine pathway



Current Pipeline



AMD1 = Adenosylmethionine decarboxylase 1; ARG1 = Arginase 1; MAT = Methionine adenosyltransferase; ODC1 = Ornithine decarboxylase 1; PAOX = Polyamine oxidase; SMO = Spermine oxidase; SMS = Spermine synthase; SRM = Spermidine synthase; SSAT = Spermidine/spermine N¹-acetyltransferase.



SBP-101

SH9 ivospemin? Sue Horvath, 2/28/2023

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

		BEST OVERA	Overall	Disease		
	CR	PR	SD	PD	Response	Control
SBP-101 (0.40 mg/kg) + G/A* (Ph Ia COHORT 2) n=7	0	5 (71%)	2 (29%)	0	5/7 (71%)	5/7 (71%)
SBP-101 (0.40 mg/kg) + G/A* (Ph Ia COHORT 4 + Ph 1b) 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		
CDD 101 (0.40 mg/kg) + C/A Cohert	Ph1a 2	Ph la 4+Ph	G+A*	Ph la 2	Ph la 4+Ph lb	G+A*
SBP-101 (0.40 mg/kg) + G/A Cohort		lb				
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

Phla = Phase la

PhIb = Phase Ib

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

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

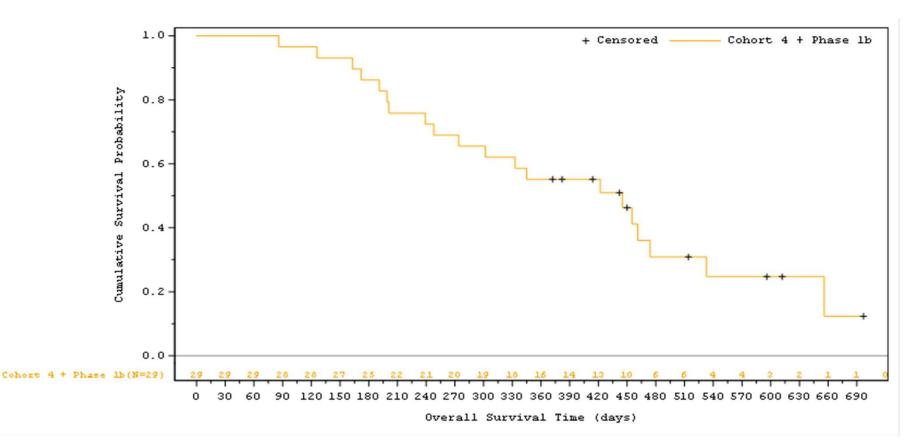
Efficacy Comparison

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

OS-Overall Survival PFS-Progression Free Survival ORR – Overall Response Rate DCR-Disease Control Rate PD – Progressive Disease

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

- One complete response (Recist)
- One clinical complete response (no detectable tumor)

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

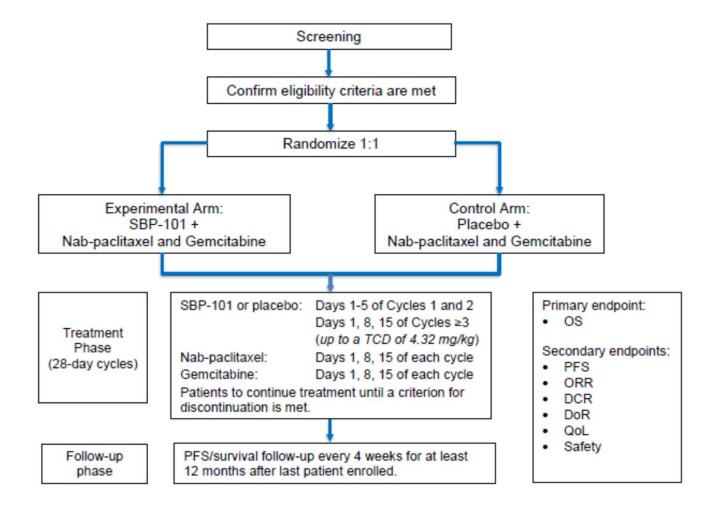
Grade ≥3 AEs of Special Interest	N	SBP- 101%		G+A %**			
Hematologic Events	Hematologic Events						
Neutropenia	20	40%		38%			
Leukopenia	0	-		31%			
Anemia	9	18%		13%			
Thrombocytopenia	1	2%		17%			
Febrile Neutropenia	1	2%		3%			
Non-hematologic Events							
Diarrhea	7	14%		6%			
Fatigue	6	12%	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

Safety Results

Grade \geq 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 <i>,</i> 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%)			

Phase III Pancreatic Cancer Trial in Subjects Previously Untreated for Metastatic SH10 Pancreatic Ductal Adenocarcinoma

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



SHould we Say ASPIRE? Sue Horvath, 2/28/2023 SH10

FLYNPOVI: A combination of CPP-1X and Sulindac

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

Familial Adenomatous Polyposis (FAP)

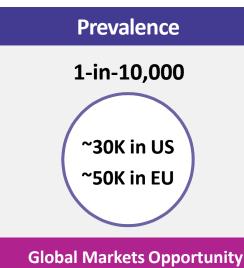
- A genetic disease caused by APC mutations where colon polyps develop early in life
- Nearly 100% of patients will develop colon cancer if the polyps are left untreated

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:

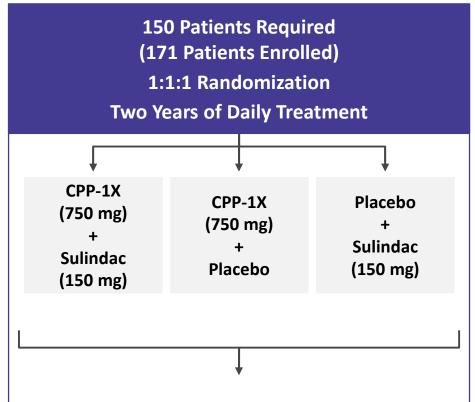
- Capped: 25% up to \$100 million in total payments
- Uncapped: 5% after capped royalty is reached

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



Endpoint "Time to FAP-related Event" (e.g., Colectomy, Duodenectomy, Spigelman score*, etc.) over at least 24 months at any Disease Site per Patient

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"

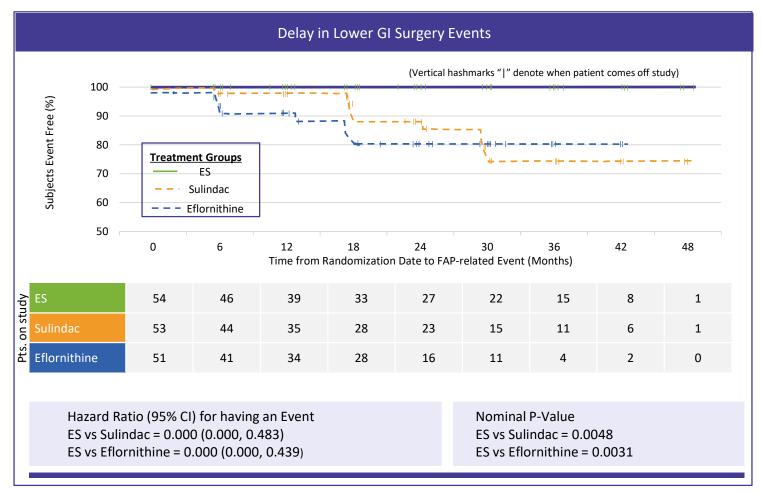
* Determined to not be a "clinically meaningful" metric resulting in a change in the clinical management or treatment for the patient Burke et al 2021 NEJM Balaguer et al 2021 DCR

No Lower GI Surgeries for Flynpovi Combination

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

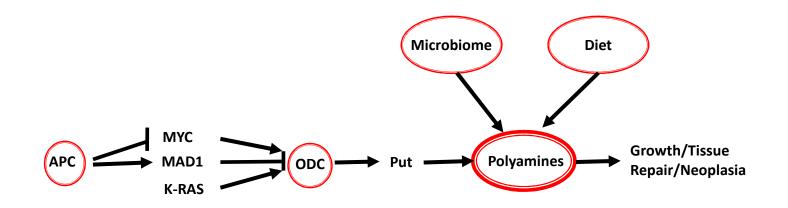
Surgery Events	ES Combo	Eflornithine	Sulindac	Overall		
	(N=56)	(N=57)	(N=58)	(N=171)		
Need colectomy	0	3	4	7		
Need proctectomy	0	1	1	2		
Need pouch resection	0	4	1	5		
Total Surgical Events	0	8	6	14		
Event Rate	0/56 (0%)	8/57 (14%)	6/58 (10%)	14/171 (8%)		
No surgeries in Lower GI in ES Combo arm						

Flynpovi Combination Delays Need for Lower GI Surgery



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

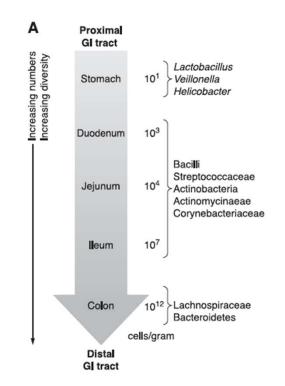
Rationale for Efficacy of Flynpovi in the Lower Gastrointestinal Tract of FAP Patients



- Polyamines drive uncontrolled growth, polyposis, and cancer.
- Polyamines can by 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 <u>nine orders of magnitude</u> (10⁹) 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

Summary of Approach to Approval

Strong Results in the Lower GI

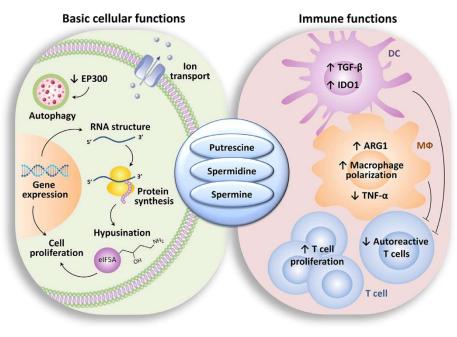
- Focus on Lower GI: statistically significant p-values and hazard ratios for clinically meaningful surgical endpoints—emphasized by regulators—in Phase III pivotal trial
- Expected safety profile over 2-4 years of daily dosing in Phase III pivotal trial
- Totality of the evidence includes mechanistic,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

No Other Approved Therapy for this Orphan Disease

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



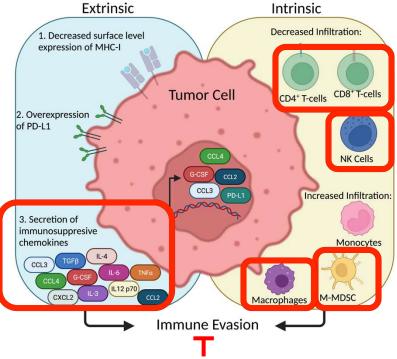
Proietti E et al 2020 Trends in Immunol

Role of Polyamines in Diffuse Large B Cell Lymphoma (DLBCL)

- MYC overexpression in relapsed/refractory DLBCL prior to CAR-T cell therapy negatively associated with durable response to CAR-T cell therapy.
- Polyamine metabolism upregulation through oncogenic MYC is a common metabolic irregularity in aggressive cancers, including lymphomas.
- Myeloid-derived suppressor cells (MDSCs) and higher IL-6 cytokine levels associated with reduced CAR-T cell expansion/poor anti-lymphoma responses after anti-CD19 CAR-T cell therapy.
- Polyamines have been reported to increase MDSCs and lead to an immunosuppresive tumor microenvironment.
- Polyamines have been shown to be important for effector function of several immune cell types including T cells.
- Circulating acetylated polyamine levels may function as a predictor of therapeutic outcome to CAR-T cell therapy.
- This suggests a possible strategy to target polyamine metabolism to augment the efficacy of CAR-T cell therapy.

Rationale for Eflornithine/anti-PD-1 Combination

- Targeting Ornithine decarboxylase (ODC) using effornithine 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 effornithine/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.





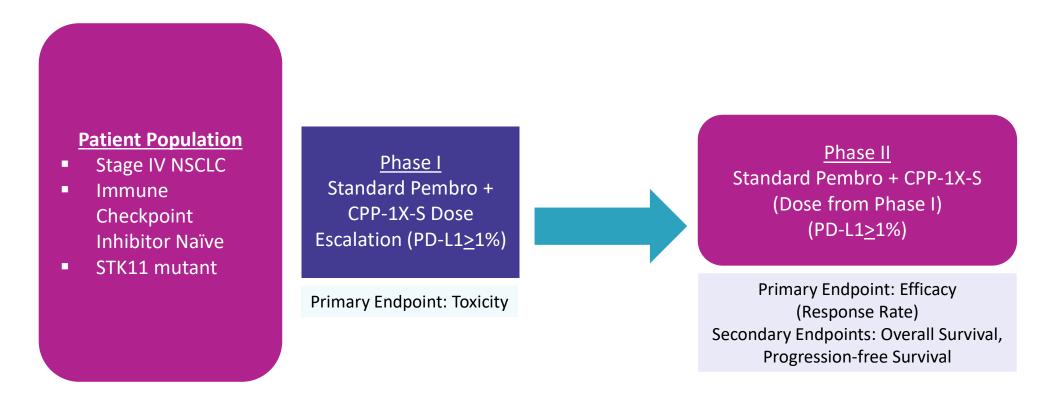
CPP-1X-S

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

- In preclinical tumor models, effornithine 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"



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



Business Overview

Barriers to Entry – Flynpovi/CPP-1X

Orphan status (7 years exclusivity US; 10 years exclusivity EU) for CPP-1X

- Granted in US and EU for FAP
- Granted in US and EU for Neuroblastoma
- Granted in US for Gastric cancer and Pancreatic cancer

Pharmaceutical Composition Patent

- Fixed dose combination effornithine + sulindac
- Broadly nationalized with potential protection through 2037

Method of Use Patents/Patent Applications

- Fixed dose combination of effornithine + sulindac and effornithine single agent
- "Theranostic" patents will afford protection to 2034 ("theranostic" = drug + diagnostic to guide therapy)
- Use in Neuroblastoma protection through 2035
- Use for Treating FAP with potential protection through 2040
- Use in Treating Recent Onset Type 1 Diabetes with potential protection through 2041
- New patents under consideration

Barriers to Entry – SBP-101

Orphan status (7 for years exclusivity US; 10 years exclusivity EU) for SPB-101

Granted in US and EU for pancreatic cancer

METHODS FOR PRODUCING (6S,15S)-3,8,13,18-TETRAAZAICOSANE-6,15-DIOL

- PCT application filed January 29, 2019
- Granted in United States, India, Japan
- Pending in United States (CON), Europe, Australia, Canada, and China
- 20-year expiration date is January 29, 2039
- DOSING REGIMENS AND METHODS FOR TREATING CANCER
 - PCT application filed January 20, 2021
 - Pending in United States, Australia, Canada and Japan
 - Filing in progress in Europe (due August 20, 2022)
 - 20-year expiration date is January 20, 2041

Summary of Milestones

1H 2023

- Open Phase I Ovarian Cancer Trial
- Open- Phase I NSCLC Trial
- Open- Neoadjuvant Pancreatic Cancer Trial
- Open Phase II Type I onset Diabetes Trial
- Futility Analysis Phase III Colon Cancer Risk Reduction Trial (PACES)
- Publication of Phase I Type I early onset Diabetes Data
- Publication of Final Phase I Metastatic Pancreatic Trial Data
- Gastric Cancer Prevention Phase II Results

2H 2023

- Open FAP Registration Trial (funded by Licensee)
- Phase I NSCLC Data
- Open Phase II NSCLC Trial

1H 2024

Overall Survival Interim Analysis Phase III ASPIRE Trial

ASCO-American Society of Clinical Oncology GI-Gastrointestinal mPC-Metastatic Pancreatic Cancer FPI-First Patient In FAP-Familial Adenomatous Polyposis NSCLC – Non Small Cell Lung Cancer

Financial Position - Cash and Debt (unaudited)

Cash and Debt	
Cash at 12/31/22	1,285,000
	1,285,000
Estimated net proceeds public sale of equity via ATM facility through 1/20/23	1,592,000
Estimated net proceeds public sale of equity on 1/30/23	13,674,000
Proforma Cash Balance ⁽¹⁾	16,551,000
Debt 12/31/22	
Current (plus accrued interest)	1,975,000
Net of current portion	5,194,000
Payments made by February 1, 2023	1,975,000

(1) Proforma Cash consists of 12/31/22 balance plus disclosed equity transactions subsequent to 12/31/22. Does not reflect any undisclosed Cash used in Operations.

Capital Stock (unaudited)

Panbela ⁽¹⁾	
Common Stock at 12/31/22	1,049,644
Shares sold via Company ATM through 1/20/23	440,830
Shares issued on 1/30/23 and Prefunded warrants exercised prior to 2/1/23	6,674,929
Shares issued in exchange for warrants through 3/31/23	7,923,913
Total Proforma Common stock outstanding	16,089,316
Shares reserved for Options (WAE = \$145.50) at 12/31/22	100,556
Shares reserved for Warrants (WAE = \$29.17) at 12/31/22	889,910
Remaining Shares (on 3/31/23) reserved for Warrants issued on 1/30/23 (EP \$2.75)	<u>2,784,776</u>
Total Proforma Outstanding and Reserved	19,864,558

(1) All Common stock, Option and Warrant amounts have been restated for 1 for 40 reverse stock split effected on 1/13/2023

Summary:

Unique Scientific Approach: Resetting dysregulation via polyamine pathway



Broad, late-stage de-risked pipeline opportunities



Multiple partnerships supporting development programs



Significant market potential



Multiple data readouts expected



Experienced management team