Investor Presentation

May 2024

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May 20, 2024

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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.

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

- Company focus on polyamine targeted platform spanning multiple indications
- Polyamine targeted therapy established in oncology with recent eflornithine approval

2

- Pipeline spans from pre-clinical to Phase III registration programs

3

- Approximately a $5 Billion aggregate market potential across lead indications

4

- Multiple near term inflection points with multiproduct, multi-indication portfolio

5

- Strategic synergies and partnerships (NCI, SWOG, JDRF, JHU SOM, MDACC, Moffitt)

Combined clinical program pipeline to create significant shareholder value

NCI-National Cancer Institute; SWOG-Southwest Oncology Group; COG-Children's Oncology Group; JDRF – Juvenile Diabetes Research Foundation; JHU SOM-Johns Hopkins University School of Medicine; MDACC-MD Anderson Cancer Center; Moffitt- Moffitt Cancer Center

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. Ashok Chavan
VP, CMC, QA, Supply Chain

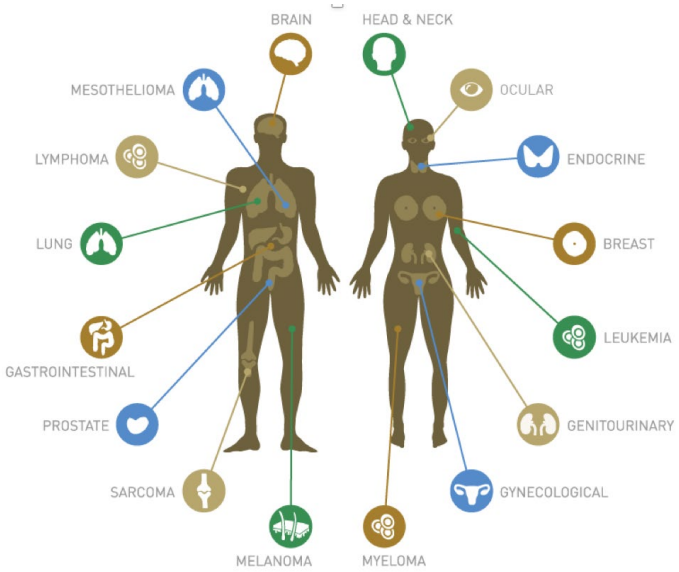
15+ Years

Rachel Bragg
VP, Clinical Development

14+ Years

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

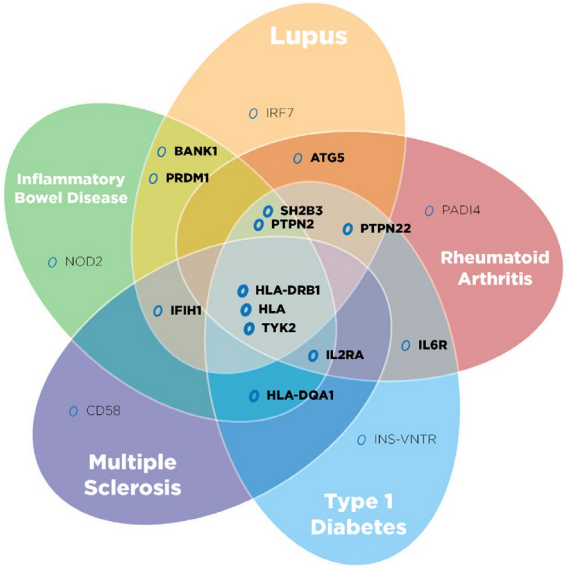
Dysregulation of the Polyamine Pathway Leads to Disease



Cancer

Pancreatic ductal adenocarcinoma
Familial Adenomatous Polyposis (FAP)
Colorectal
Ovarian
STK11 Mutant NSCLC
Prostate
Neuroblastoma*

Polyamine Dysregulation in Disease



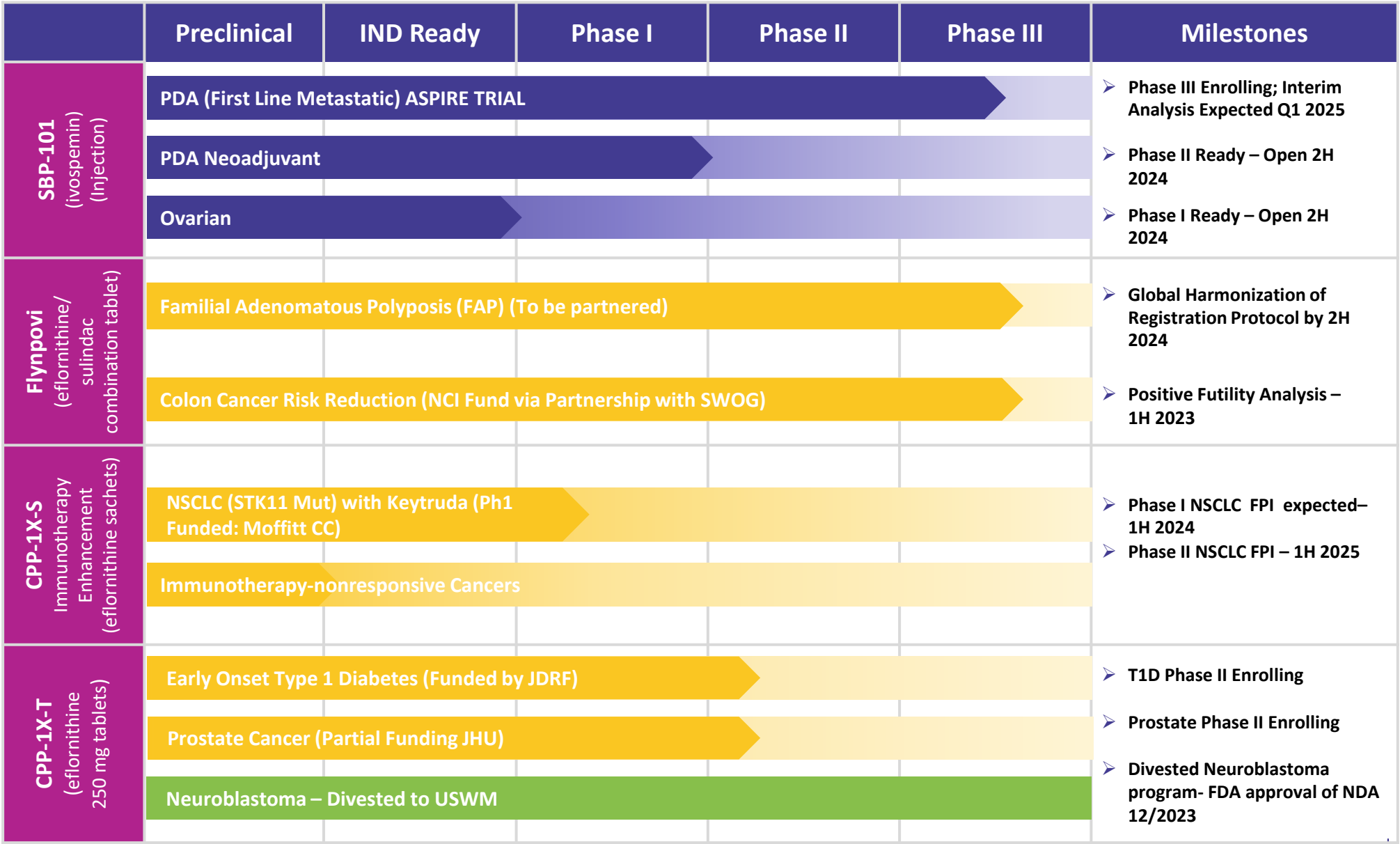
Autoimmune Diseases

Recent Onset Type 1 Diabetes

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
*Neuroblastoma program divested to USWM received FDA approval of NDA 12/2023

Pipeline: Addresses Multiple Unmet Needs



PDA – Pancreatic Ductal Adenocarcinoma; FPI-First Patient In

Potential $5B Market Opportunity for Lead Programs

Pancreatic Cancer	FAP	Colorectal Cancer	Ovarian Cancer
Incidence of Pancreatic Cancer 64K in US ~151K in EU	Incidence of FAP ~30K in US ~50K in EU	Incidence of Colorectal Cancer ~150K in US ~340K in EU	Incidence of Ovarian Cancer ~22K in US ~79K in EU
~215K	**~80K**	**~490K**	**~101K**
1L Metastatic Pancreatic Cancer Target Population ~37K in US ~96K in EU	FAP Prevalence[1] and Target Population ~15K in US ~20K in EU	5-year prevalence[2] Colorectal Cancer Target Population ~400K in US ~950K in EU	Ovarian Cancer Target Population ~12K in US ~46K in EU
~133K	**~35K**	**~1.35M**	**~58K**
Approximately 70% of MPDA patients are treated.			Approximately 58% patients are late stage at diagnosis

FAP Source: Burt et al 2010; Varesco et al 2004; multiple KOL sources.
Pancreatic Cancer Source: American Cancer Society. Cancer Facts & Figures 2023. Atlanta, GA: American Cancer Society; 2023 and Overview of Pancreatic Cancer Epidemiology in Europe and Recommendations for Screening in High-Risk Populations, Partyka, et al July 2023.
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

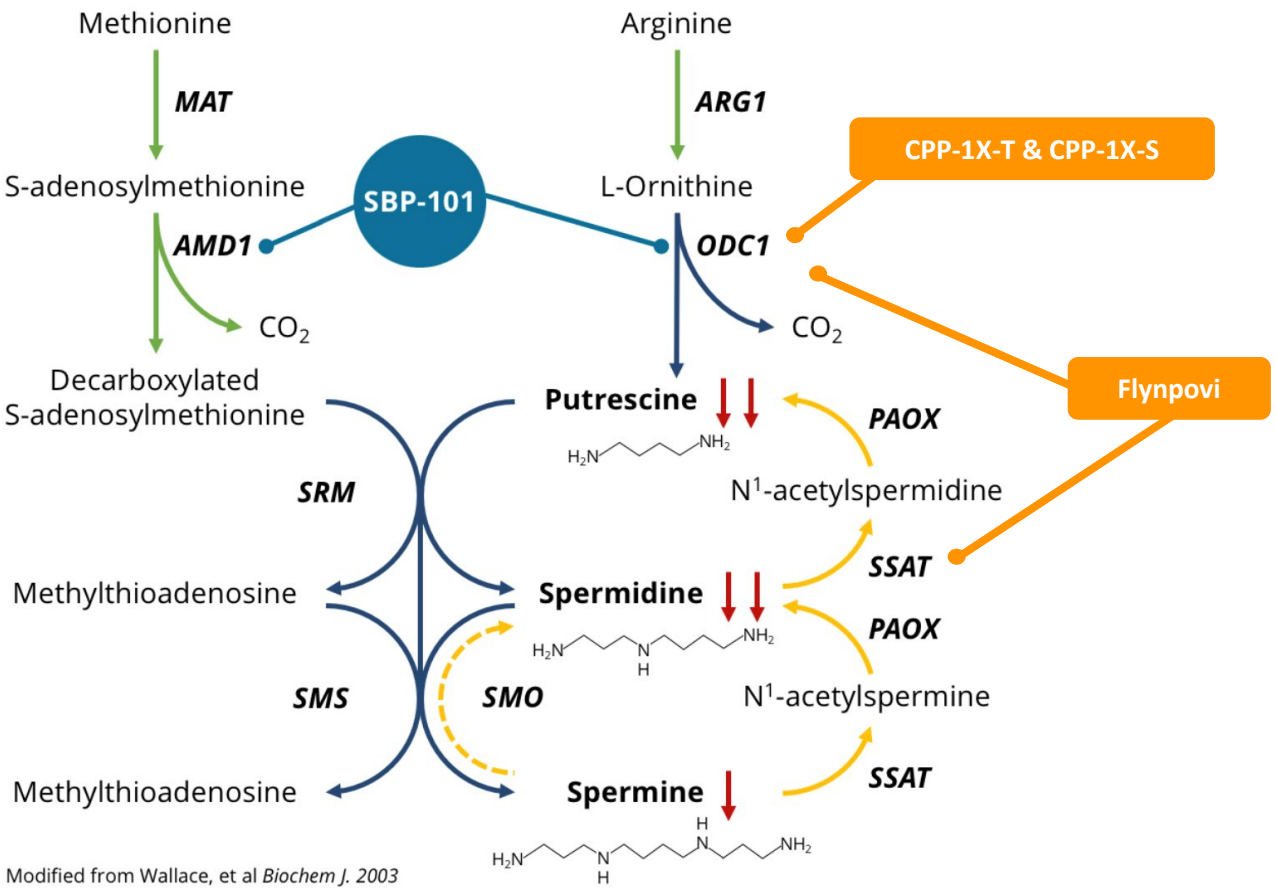
Pipeline Objective

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

Current Pipeline

1. Ivospemin (SBP-101)
2. Flynpovi
3. CPP-1X-T
4. CPP-1X-S

Combined pipeline pharmacotherapies hit different targets in the polyamine pathway



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 N^1-acetyltransferase.

Ivospemin (SBP-101)

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

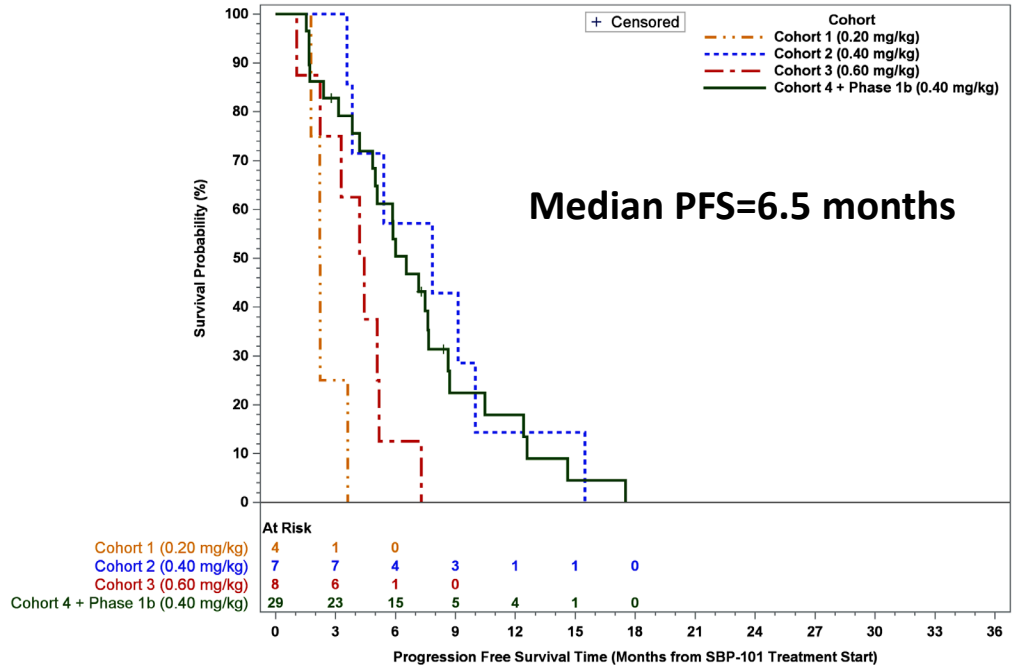
	BEST OVERALL RESPONSE				Overall Response	Disease Control
	CR	PR	SD	PD		
ivospemin (0.40 mg/kg) + G/A* (Ph Ia COHORT 4 + Ph 1b) n=29	1 (3%)	13 (45%)	10 (34%)	5 (17%)	**14/29 (48%)**	**24/29 (83%)**
Gemcitabine + Nab-paclitaxel (G/A*) n=431**	<1%	23%	27%	20%	**23%**	**48%**

	PFS			OS		
ivospemin (0.40 mg/kg) + G/A Cohort	**Ph Ia 4+Ph Ib**	G+A** mPACT	G+A† NAPLOI 3	**Ph Ia 4+Ph Ib**	G+A** mPACT	G+A† NAPOLI 3
Median (mo)	**6.5**	5.5	5.6	**14.6*****	8.5	9.2
6 mo (%)	**54**	44	43.2	**86**	67	68.4
12 mo (%)	**18**	16	13.9	**55**	35	39.5

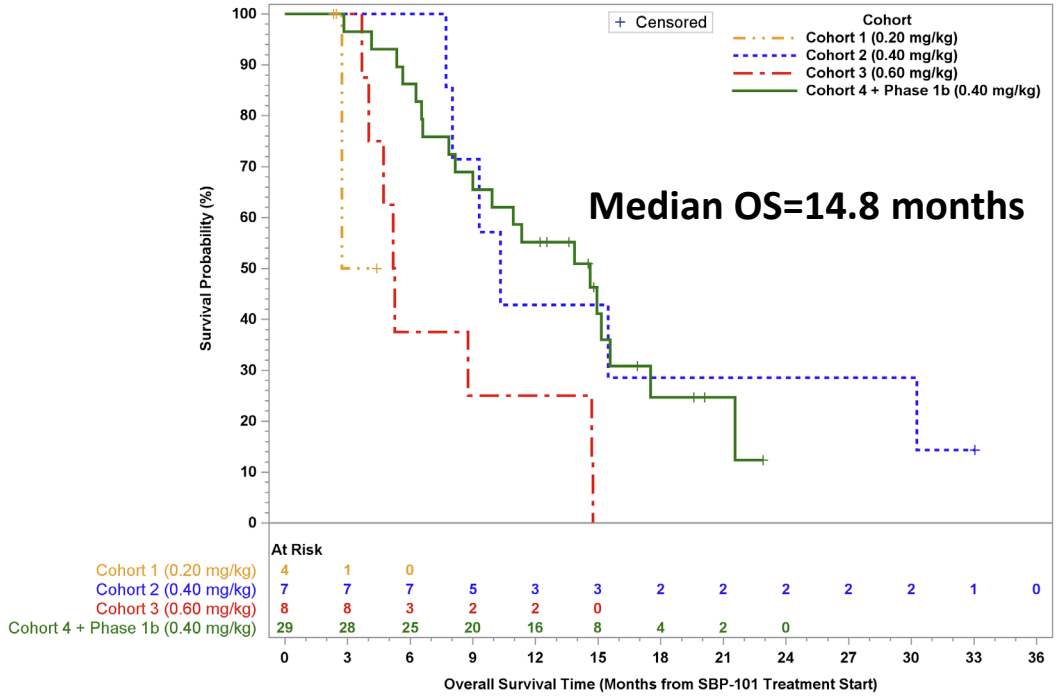
*G/A = gemcitabine + Nab-paclitaxel
**Historical control data, MPACT study G+A arm, N=431 - Source: Von Hoff NEJM 2013
†NAPLOI 3 Trial G=A arm, N=387 – Source: Wainberg et al LANCET 2023
*** Final Data–3/18/22
PhIa = Phase Ia
PhIb = Phase Ib
CR-Complete Response; PR-Partial Response; SD-Stable Disease
Disease Control Rate = CR+PR+SD for > 16 weeks

Phase I Trial Efficacy of SBP-101 +Gemcitabine/Nab-paclitaxel

Progression-Free Survival (PFS)



Overall Survival (OS)



- Cumulative survival rates at 6 and 12 months were 86.2% and 55.2%. with 3 subjects (10.3%) alive at 19.6, 20.1, and 22.9 months.
- The cumulative PFS rates were 54.0% and 17.9% at 6 and 12 months.
- Nine (31%) subjects treated at the RD were alive at the time of data analysis and were censored for OS. These subjects were alive for an average of 16.4 months (range 12.2 – 22.9 months)

RD=Recommended dose

Ivospemin (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%

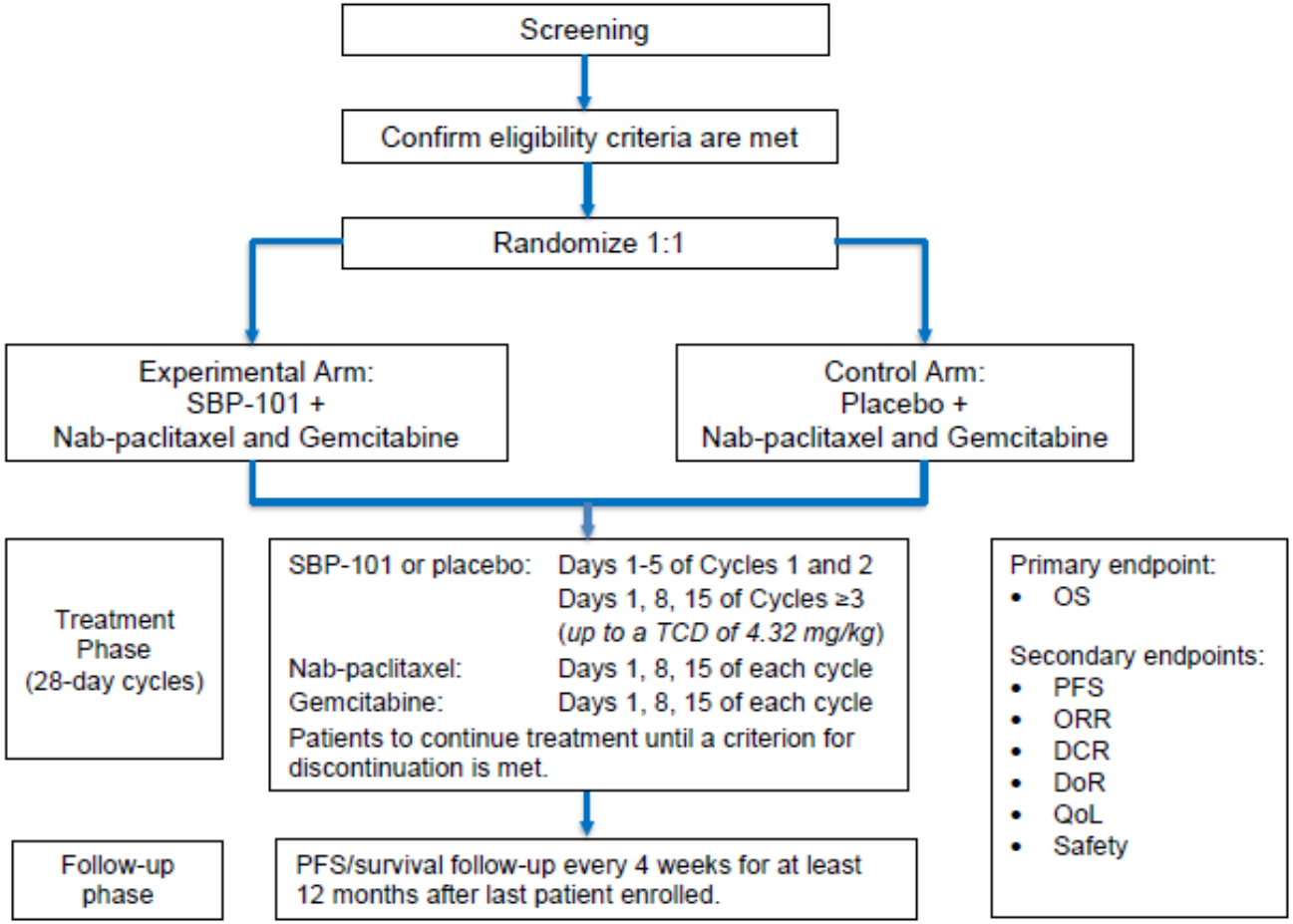
Grade ≥3 adverse events attributable to any study medication, N=50.				
Event	SBP-101	G+A**	All 3	Total N (%)
Neutropenia	0	19 (1G, 18 G+A)	1	20 (40%)
Elevated LFTs	5	0	9	14 (28%)
Anemia	0	7 (G+A)	0	9 (18%)
Diarrhea	0	6 (4A, 2G+A)	1	7 (14%)
Fatigue	0	4 (G+A)	2	6 (12%)
Vision events	4	1 (G)	2	7(14%)
Dehydration	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 III Pancreatic Cancer Trial in Subjects Previously Untreated for Metastatic Pancreatic Ductal Adenocarcinoma

ASPIRE Clinical Research Study

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



OS-Overall Survival
PFS-Progression Free Survival
ORR – Overall Response Rate
DCR-Disease Control Rate
DoR – Duration of Response
QoL-Quality of Life

Efficacy Comparison of ivospemin (SBP-101) + Gemcitabine/Nab-paclitaxel vs. Standard of Care

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%
NALIRIFOX - Phase I/II (NAPOLI 3)[4]	12.6 months	9.2 months	34.4%	71.9 %	9.4%
NALIRIFOX - Phase III (NAPOLI 3)[4]	11.1 months	7.4 months	41.8%	67.6%	10.0%
Gemcitabine + Abraxane – Phase I/II[5]	12.2 months	7.9 months	48%	68%	16%
Gemcitabine + Abraxane Phase III (MPACT)[6]	8.5 months	5.5 months	23%	48%	20%
Gemcitabine + Abraxane- Phase III (NAPOLI 3)[4]	9.2 months	5.6 months	36.2%	62.3%	15.0%

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. Wainberg et al, 2023;
5. Von Hoff et al, 2011;
6. Von Hoff et al, 2013

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

Summary of First Line Metastatic Pancreatic Cancer FDA Approvals

- ✓ MPACT Trial
  - ✓ Gemcitabine + Abraxane vs Gemcitabine N=831
  - ✓ Median OS Benefit: 1.8 months (G+A 8.5 months vs Gemcitabine 6.7 months)
  - ✓ FDA Approval 2013– Gemcitabine + Abraxane
- ✓ NAPOLI 3 Trial
  - ✓ liposomal irinotecan in combination with fluorouracil, leucovorin, and oxaliplatin (NALIRIFOX) vs Gemcitabine + Abraxane, N=770
  - ✓ Median OS Benefit: 1.9 months (NALIRFOX 11.2 vs G+A 9.2 months)
  - ✓ FDA Approval 2024 – Onivyde (liposomal irinotecan) in combination with fluorouracil, leucovorin, and oxaliplatin

Positive Movement in the Treatment of First Line Metastatic Pancreatic Cancer

FLYNPOVI:
A Combination of CPP-1X and Sulindac

Familial Adenomatous Polyposis (FAP): 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
  - ✓ No surgeries in the lower GI group over 2-4 years
- ✓ 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
- ✓ Seek partner to optimize program

No Other Approved Therapy for this Orphan Disease

CPP-1X-S

Targeting Type 1 Diabetes Using POLyamines (TADPOL)

A Randomized, Double-Masked, Placebo-Controlled Phase 2 Study

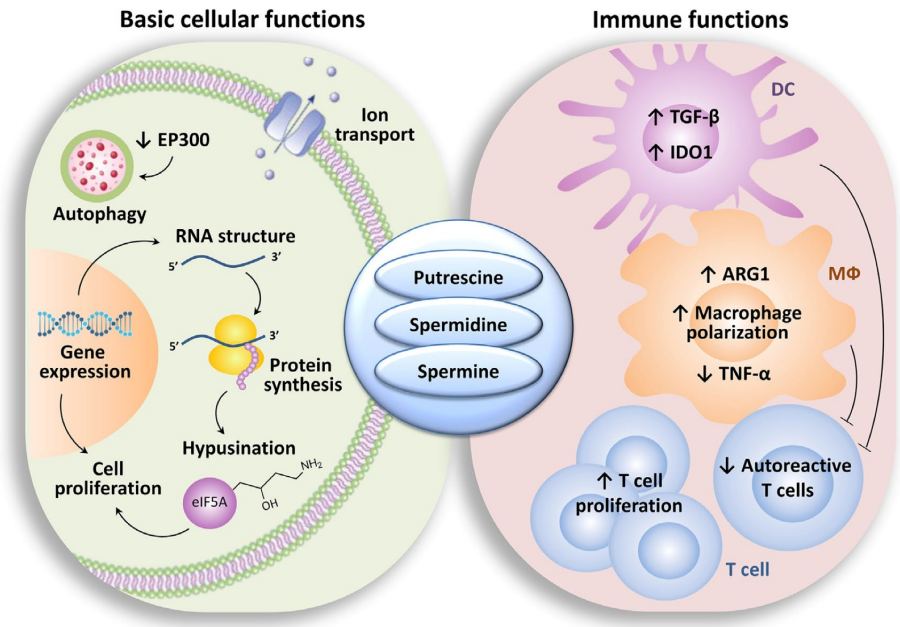
- ✓ Evaluate the Efficacy and Safety of DFMO (eflornithine) to Preserve Insulin Production in Type 1 Diabetes
- ✓ N=70
- ✓ Multicenter, led by Indiana University School of Medicine
- ✓ Funded by JDRF

Well designed phase 2 study may lead to significant opportunity in Type 1 Diabetes market

Polyamines & Immune Dysregulation

Role of Polyamines in Immune Dysregulation

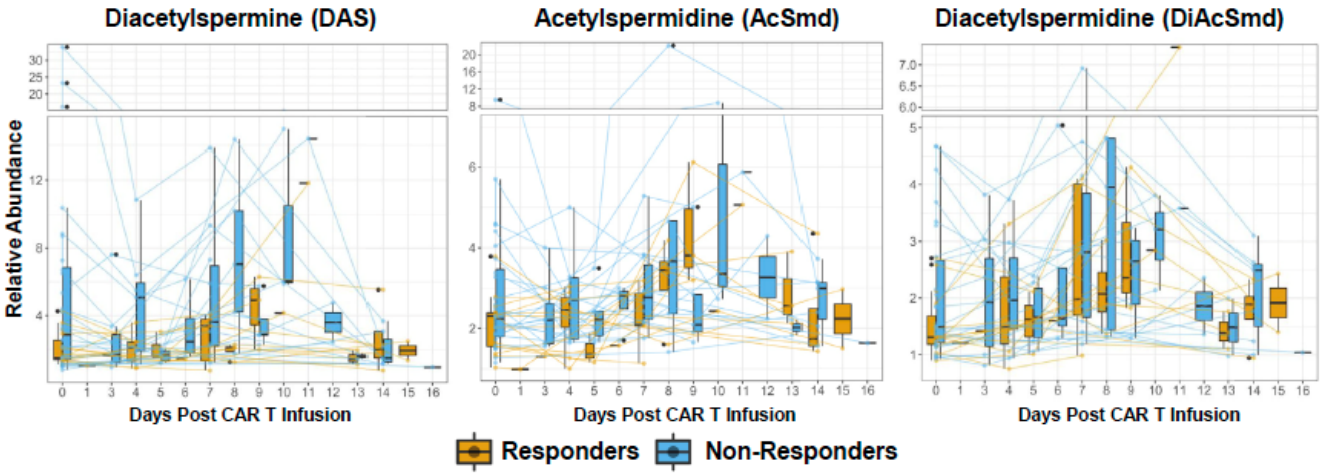
- Immune systems require multiple soluble and cellular components, including polyamines, for a normal immune function
- High levels of polyamines are present in tumor cells and in autoreactive B- and T-cells in autoimmune diseases
- Dysregulation of polyamines can result in:
  - Tumor immune evasion
  - 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

Potential Role of Polyamines in Diffuse Large B Cell Lymphoma (DLBCL) CAR-T Therapy

- Polyamine metabolism upregulation through oncogenic MYC is a common metabolic irregularity in aggressive cancers, including lymphomas.
- MYC overexpression in relapsed/refractory DLBCL prior to CAR-T cell therapy negatively associated with durable response to CAR-T cell therapy.
- 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.

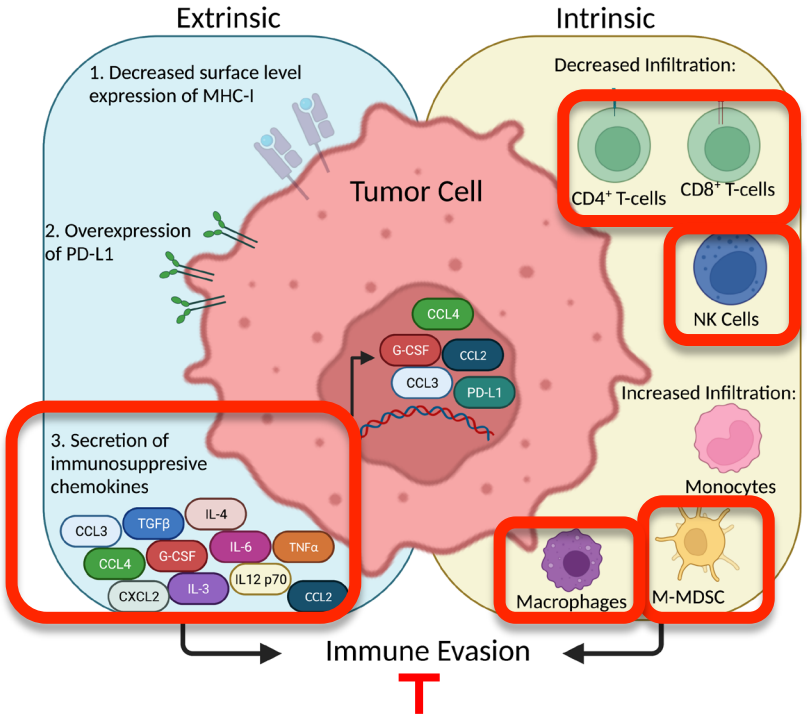


Intra-patient slopes considering random variables for intercept and slope			
Metabolite	**Responders**	**Non-Responders**	**Pval**
DAS	-0.077 (-0.107 to -0.065)	0.086 (0.062 to 0.115)	<0.0001
AcSpmd	0.028 (0.013 to 0.048)	0.074 (0.057 to 0.087)	<0.0001
DiAcSpmd	0.034 (0.020 to 0.034)	0.069 (0.057 to 0.078)	<0.0001

Fahrmann JF et al 2022 Cell Reports Medicine

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.**



Modified from Tanaka M et al 2020 Cancers

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

Cancer Genomic Atlas Research 2014 Nature
Skoulidis F et al 2018 Cancer Discov
Skoulidis F et al 2019 JCO
Dryia P et al 2021 J Immunother
Alexander Et et al 2020 Mol Cancer Ther

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≥1%)

Primary Endpoint: Toxicity

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

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

First Clinical Proof of Concept for Polyamine Modulation of the Immune System

PD-L1-programmed death ligand-1

USWorld Medicines Neuroblastoma Program

Anticipated Milestones from USWM Neuroblastoma Program

FDA granted approval to eflornithine (IWILFIN) as a treatment for adult and pediatric patients with high-risk neuroblastoma (HRNB) who have achieved a partial response or better to a previous, multiagent, multimodal treatment including an anti-GD2 immunotherapy

- First polyamine targeted therapy approved in oncology

Milestones:

- Up to $7.6M remaining in milestone payments related to clinical development, regulatory approval and commercial sales.

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 for Gastric cancer and Pancreatic cancer
- **Pharmaceutical Composition Patent**
  - Fixed dose combination eflornithine + sulindac
  - Broadly nationalized with potential protection through 2037
- **Method of Use Patents/Patent Applications**
  - Fixed dose combination of eflornithine + sulindac and eflornithine single agent
  - "Theranostic" patents will afford protection to 2034 ("theranostic"= drug + diagnostic to guide therapy)
  - 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 – ivospemin (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, United States (CON), India, Japan, Australia, Europe, China
  - Pending in Canada
  - 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, Japan, Europe, and Hong Kong
  - 20-year expiration date is January 20, 2041

- **COMBINATION TREATMENT FOR OVARIAN CANCER**
  - PCT application filed June 21, 2023

Summary of Milestones

1H 2024

- FPI NSCLC Phase 1 Trial
- Gastric Cancer Prevention Phase II Results

2H 2024

- Open- Neoadjuvant Pancreatic Cancer Trial
- Open Phase 1 Ovarian Trial
- Obtain feedback from FDA and EMA for Global Registration Program in FAP
- **Publication of Final Phase 1 Metastatic Pancreatic Trial Data**

1H 2025

- **Overall Survival Interim Analysis Phase III ASPIRE Trial**
- Open NSCLC Phase II Trial

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 3/31/2024	262
Cash received after 3/31/2024	775
Proforma net cash as of 3/31/2024	1,037
Debt at 3/31/2024	
Current (Due January 31, 2025)	1,000,000
Non-current	3,194,000
Total	4,194,000

Capital Stock (unaudited)

Panbela	
Common Stock issued and outstanding at 3/31/2024	4,854,861
Shares reserved for Options (WAE = $14,410.38) at 3/31/2024	607
Shares reserved for Warrants (WAE = $3.13) at 3/31/2024	9.095.943
Total Proforma Outstanding and Reserved	**13,951,411**

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