Panbela™
THERAPEUTICS

Company Overview

March 2022

Last modified on
3/21/22

Cautionary Statements

Certain statements in this presentation are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and are provided under the protection of the safe harbor for forward-looking statements provided by that Act. Forward-looking statements are based on current expectations of future events and often can be identified by words such as “anticipate,” “believe,” “continue,” “estimate,” “expect,” “future,” “intend,” “may,” “plan,” “potential,” “target,” or other words of similar meaning or the use of future dates. Examples of forward-looking statements include future determinations of the characteristics of SBP-101 and its effectiveness, publication of results, other trial activities and the timing of the same, and expected financial or operating results. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our beliefs, expectations, and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially and adversely from the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the following: (i) our lack of diversification and the corresponding risk of an investment in our Company; (ii) potential deterioration of our financial condition and results due to failure to diversify; (iii) our ability to successfully complete acquisitions and integrate operations for new product candidates; (iv) our ability to obtain additional capital, on acceptable terms or at all, required to implement our business plan; (v) final results of our Phase 1 clinical trial; (vi) progress and success of our randomized Phase 2/3 clinical trial; (vii)our ability to demonstrate safety and effectiveness of our product candidate; (vii) our ability to obtain regulatory approvals for our product candidate in the United States, the European Union or other international markets; (viii) the market acceptance and future sales of our product candidate; (ix) the cost and delays in product development that may result from changes in regulatory oversight applicable to our product candidate; (x) the rate of progress in establishing reimbursement arrangement with third-party payors; (xi) the effect of competing technological and market developments; (xii) the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims; and (xiii) such other factors as discussed in Part I, Item 1A under the caption “Risk Factors” in our most recent Annual Report on Form 10-K, any additional risks presented in our subsequent Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Any forward-looking statement made by us in this presentation is based on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement or reasons why actual results would differ from those anticipated in any such forward-looking statement, whether written or oral, whether as a result of new information, future developments or otherwise.

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 Highlights

New Therapeutic Class For Solid Tumors

- Developing small molecule polyamine metabolic inhibitors with tumor and organ-specific preferential uptake
- Multiple cancer types with known elevated polyamine levels represent potential targets
- Novel Trojan Horse polyamine metabolic inhibitor (PMI) mechanism and tolerability profile seen in early studies may enable use in combination with other agents
- *Potential dual attack:* growth inhibition + relieve polyamine-mediated immune suppression

SBP-101 Combination Therapy for First Line Metastatic Pancreatic Cancer

- Pancreatic ductal adenocarcinoma (PDA) has the lowest survival rate among major cancers
- Fast track and orphan designation from FDA; SBP-101 is administered subcutaneously
- SBP-101 given first line with standard of care in Cohort 4 + Phase 1B study interim results:
  - 48% objective response rate; more than double historical standard of care
  - 70% of patients with CA 19-9 biomarker reductions of greater than 60%
  - Enrollment ended December 2020; 7 patients remain in survival follow-up

Strong Foundation & Management Team

- Raised ~$47M in capital since inception to fund SBP-101 development
- Randomized Phase 2/3 initiated January 2022
- Patent issued Aug 2021 for improved, exclusive synthetic process
- High quality management with proven oncology drug discovery, development and commercialization expertise

Panbela Leadership Team and Board of Directors

- Collectively developed 10 FDA-approved therapies generating billions in sales

Leadership Team

Jennifer K. Simpson, PhD, MSN, CRNP
President & CEO

Susan Horvath, CPA (inactive), CMA
VP of Finance & CFO

Thomas X. Neenan, PhD
Co-Founder, Chief Scientific Officer

Rachel Bragg, MPH
VP, Clinical Development

Michael Walker, MD
Senior Medical Director, Clinical Research

Tammy Groene
VP, Operations

Board of Directors

Michael T. Cullen, MD, MBA, ABIM

Jennifer K. Simpson, PhD, MSN, CRNP

Art Fratamico, MBA

Suzanne Gagnon, MD, FACP

Jeff Mathiesen, CPA

Paul W. Schaffer, PharmD

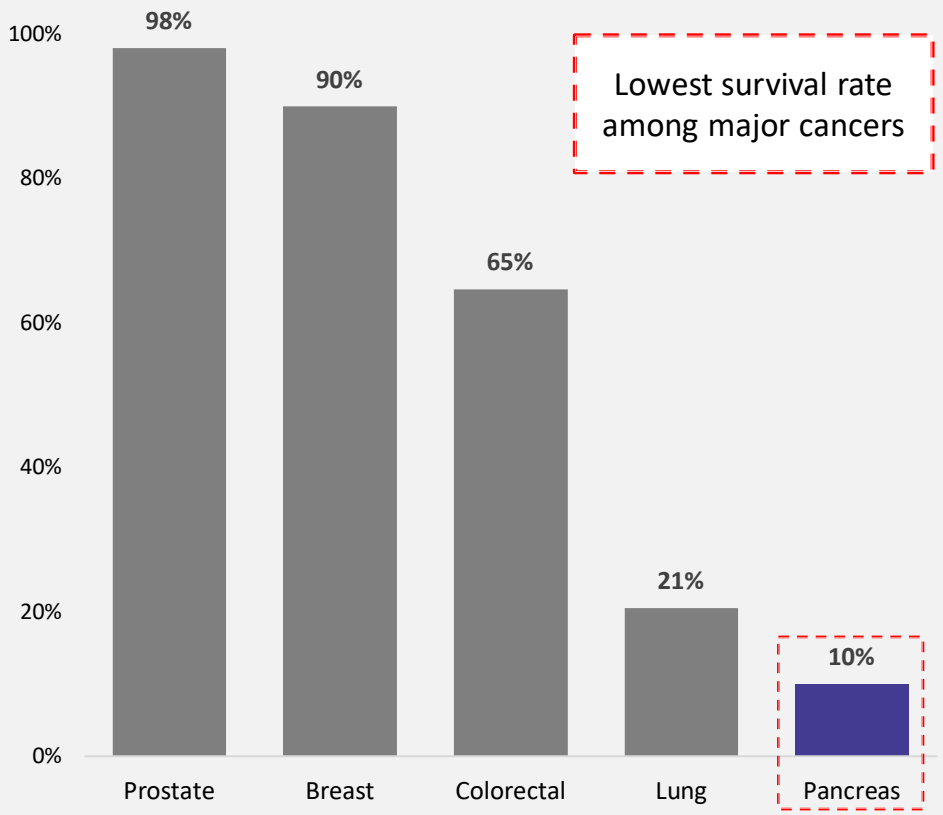
D. Robert Schemel

Proven oncology drug discovery, development and commercialization expertise

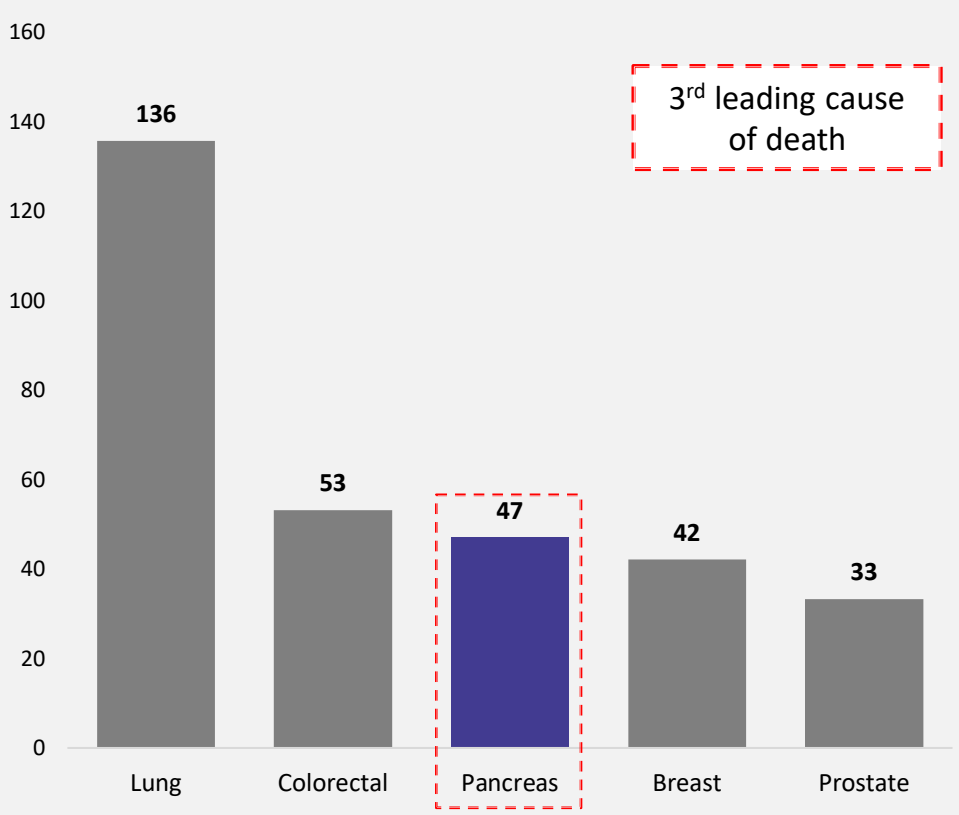
Pancreatic Cancer: a Major Unmet Medical Need

- Globally, the number of deaths caused by, and incidence of, pancreatic cancer has more than doubled from 1990 to 2017

5-Year Survival Rate (U.S.)



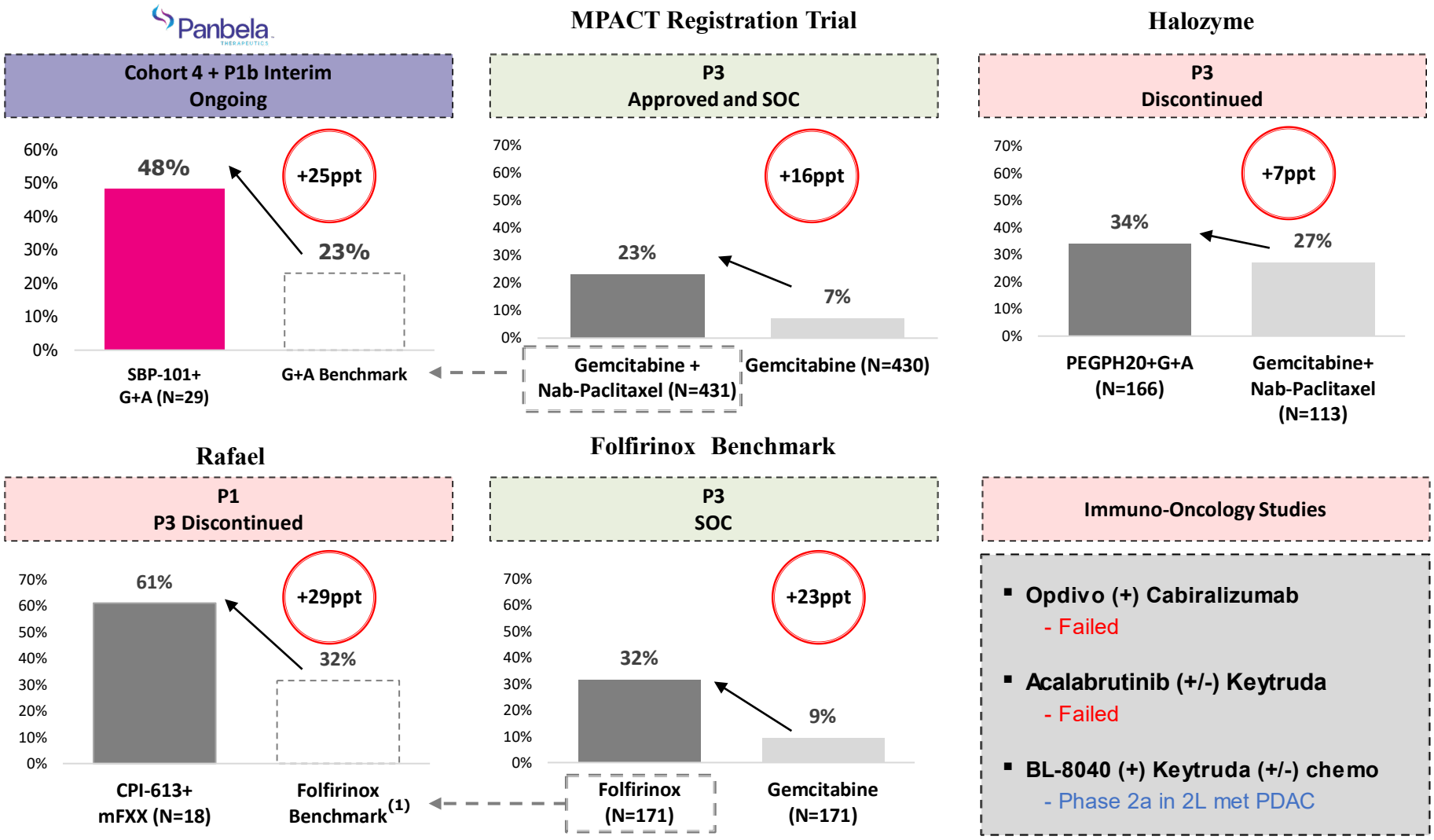
Deaths in the U.S. (Thousands)



Sources: *www.seer.cancer.gov referenced July 24, 2020 &*
"Global Burden of Disease Cancer…" JAMA Oncology, American Medical Association, 1 Nov. 2018

Objective Response Rate Comparison Among Prior PDAC Trials

- In addition to strong ORR results, 70% of SBP-101 patients presented CA 19-9 biomarker reductions of greater than 60%



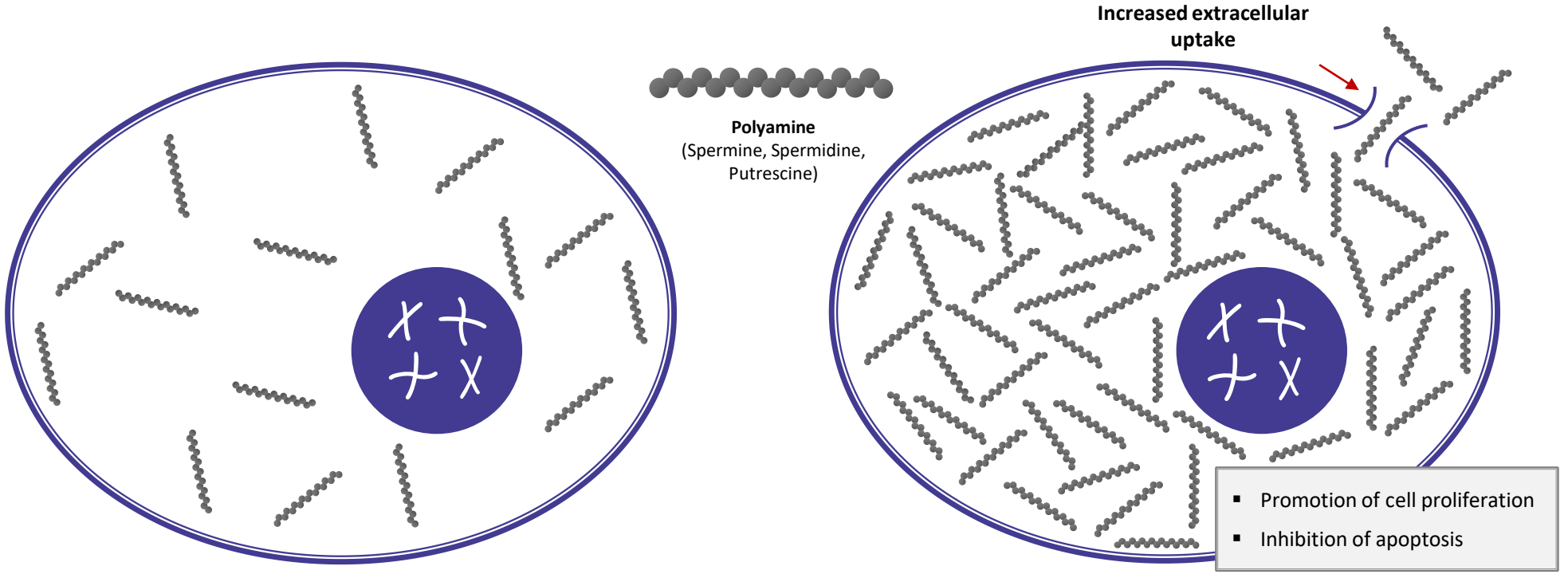
(1) Comparison not apples to apples - CPI-613 was used in combination with a modified Folfirinox, which excluded bolus fluorouracil

Increased Polyamine Levels Can Enhance the Malignant Potential of Cancer Cells and May Decrease Anti-Tumor Immunity

- Many tumors maintain greatly elevated levels of polyamines to support their rapid growth and survival
  - Of all human tissues, the pancreas has the highest level of native spermidine creating a polyamine rich environment for proliferation
  - Oncogenes such as MYC & RAS upregulate polyamine synthesis & increase cellular uptake by inducing the polyamine transport system
- Polyamines also act as immune suppressants inhibiting T-cells, monocytes, and macrophages

Healthy Cell
(Low Polyamine Levels)

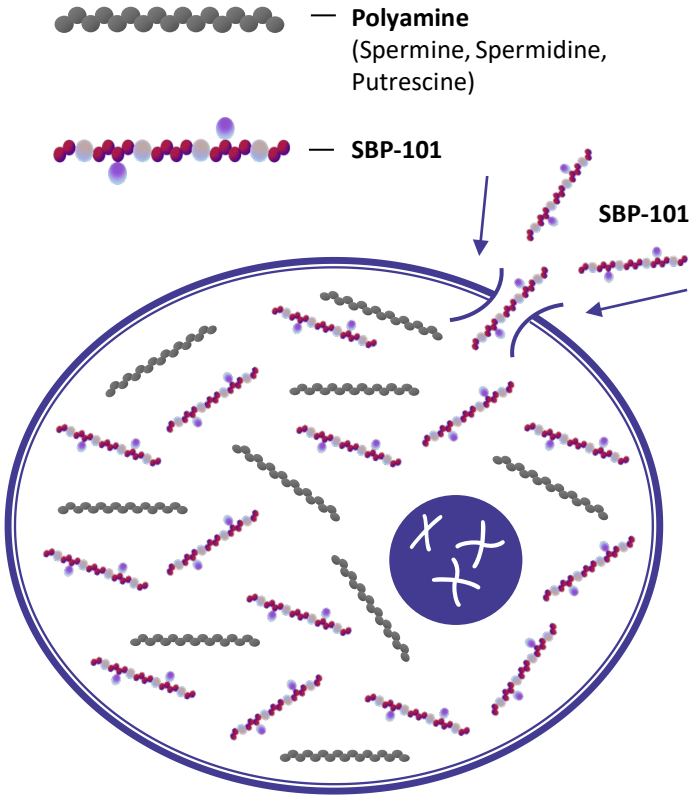
Cancer Cell
(High Polyamine Levels)

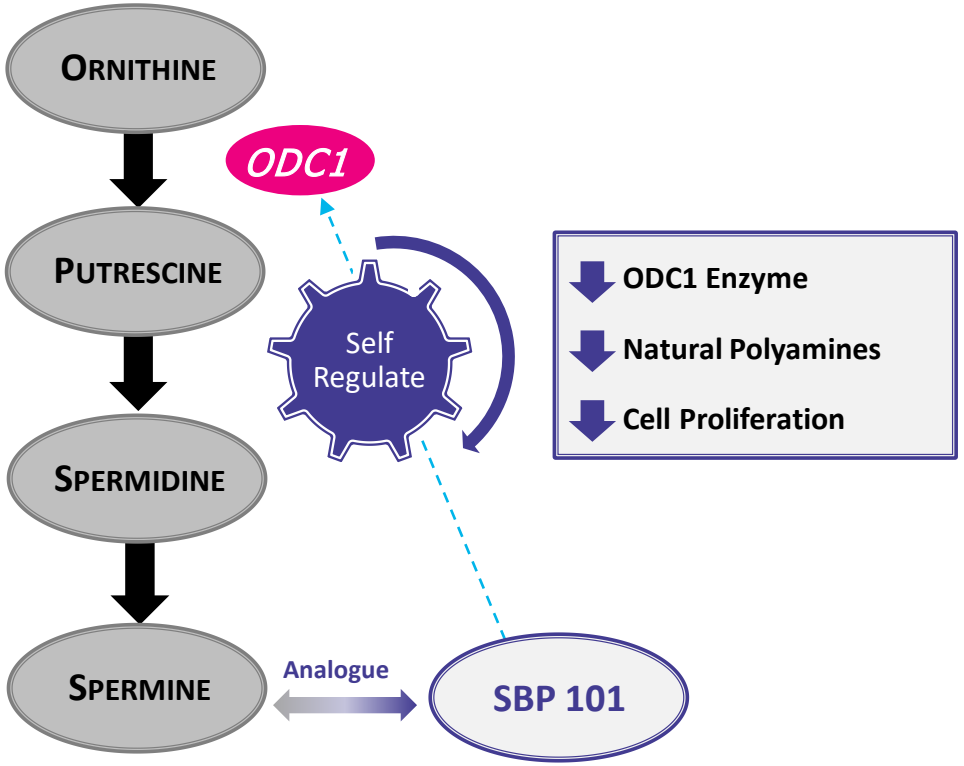


SBP-101 MOA (Trojan Horse): Synthetic Polyamine Analogue

- SBP-101 is a synthetic analogue of spermine being designed to exploit the self-regulating nature of polyamine metabolism
- SBP-101 preferentially accumulates in tumor cells and downregulates the polyamine metabolic pathway, lowering production of the natural polyamine pool and inhibiting cell proliferation
- In investigational studies, SBP-101 does not trigger a polyamine catabolic cascade or the creation of harmful reactive oxygen species

SBP-101 Taken Up Extracellularly *And….* **Downregulates Upstream Production of ODC1**





SBP-101 Phase 1 PDA Study Design*

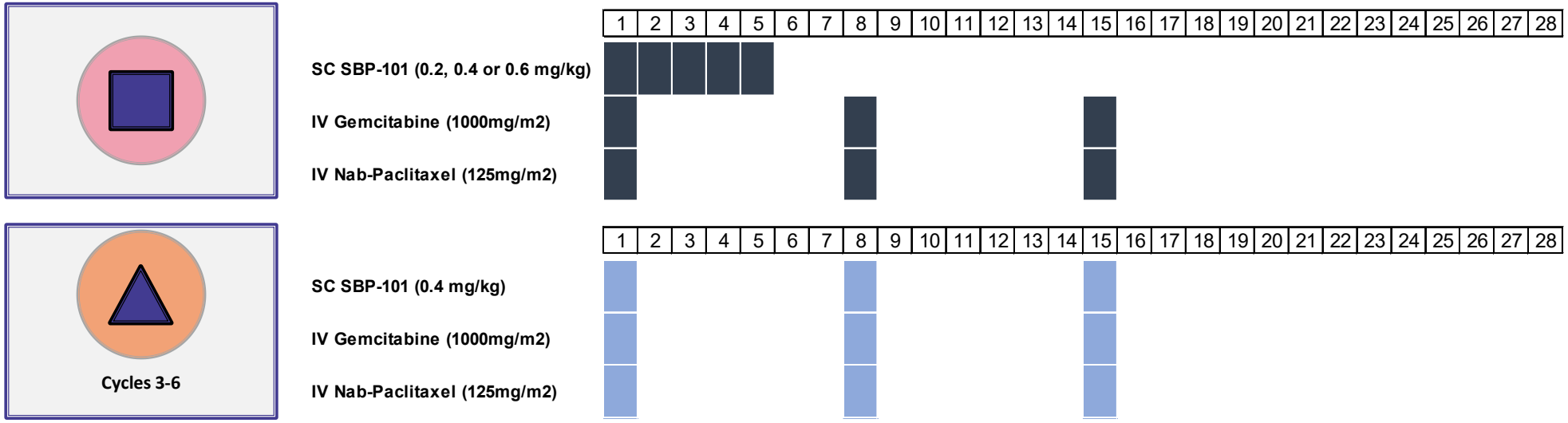
Overview

- Open-label P1A/1B study to assess safety, tolerability and PK when combined with Nab-Paclitaxel and Gemcitabine
- Identify P2 dose and schedule and assess preliminary efficacy of 3-drug treatment combination
- **Primary Outcome Measure**
  - Safety, PK, Tolerability
- **Areas of Exploration**
  - Overall Response Rate, CA 19-9 Levels, Progression-Free Survival

Design

	Dose	Enrolled	Dosing Schedule
Cohort 1 (n = 4)	0.2 mg/kg	✓	■ only
Cohort 2 (n = 7)	0.4 mg/kg	✓	■ only
Cohort 3 (n = 9)	0.6 mg/kg	✓	■ only
Cohort 4 (n = 5)	0.4 mg/kg	✓	2 ■ + 4 ▲
Expansion Cohort (n = 25)	0.4 mg/kg	✓	2 ■ + 4 ▲

Treatment Spans Up to Six 28-Day Cycles

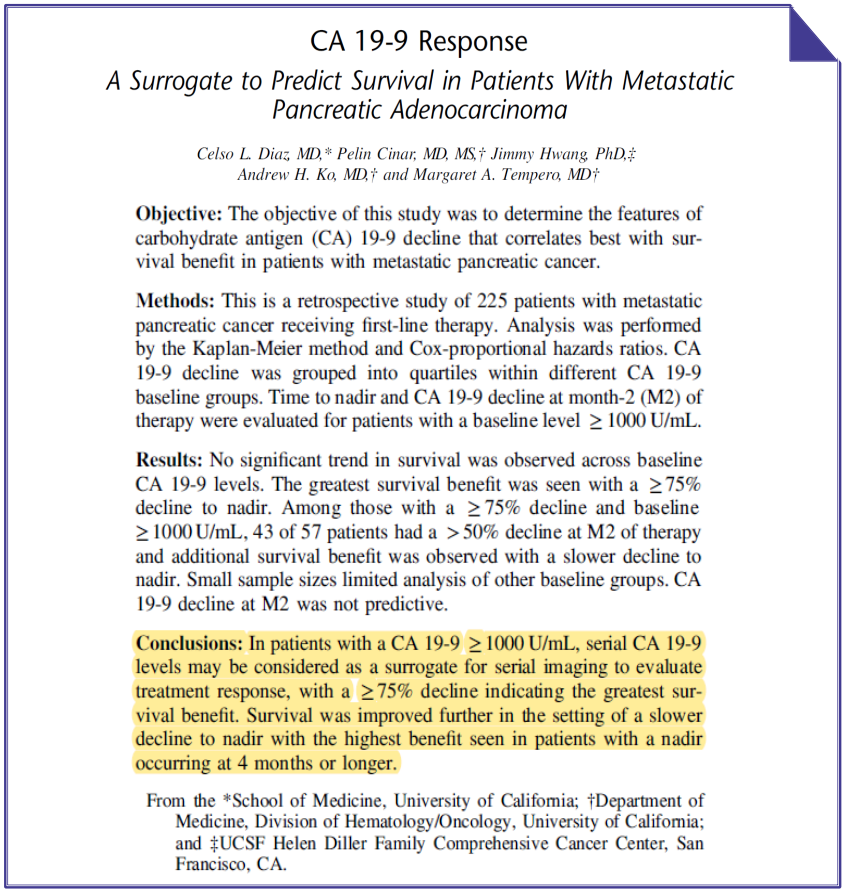


www.clinicaltrials.gov NCT03412799

*Phase 1 trial on Partial Clinical Hold from 2/21 until 4/21

Clinical Importance of CA 19-9 Biomarker

- Carbohydrate antigen (CA) 19-9 is a type of antigen found in the blood that is often elevated in pancreatic disease
- Studies have suggested that decreases in CA 19-9 levels are correlated with improved prognosis; ≥60-75% declines in CA 19-9 levels correlated with the greatest survival benefit in pancreatic cancer



CA 19-9 Response

A Surrogate to Predict Survival in Patients With Metastatic Pancreatic Adenocarcinoma

Celso L. Diaz, MD, Pelin Cinar, MD, MS,† Jimmy Hwang, PhD,‡ Andrew H. Ko, MD,† and Margaret A. Tempero, MD†*

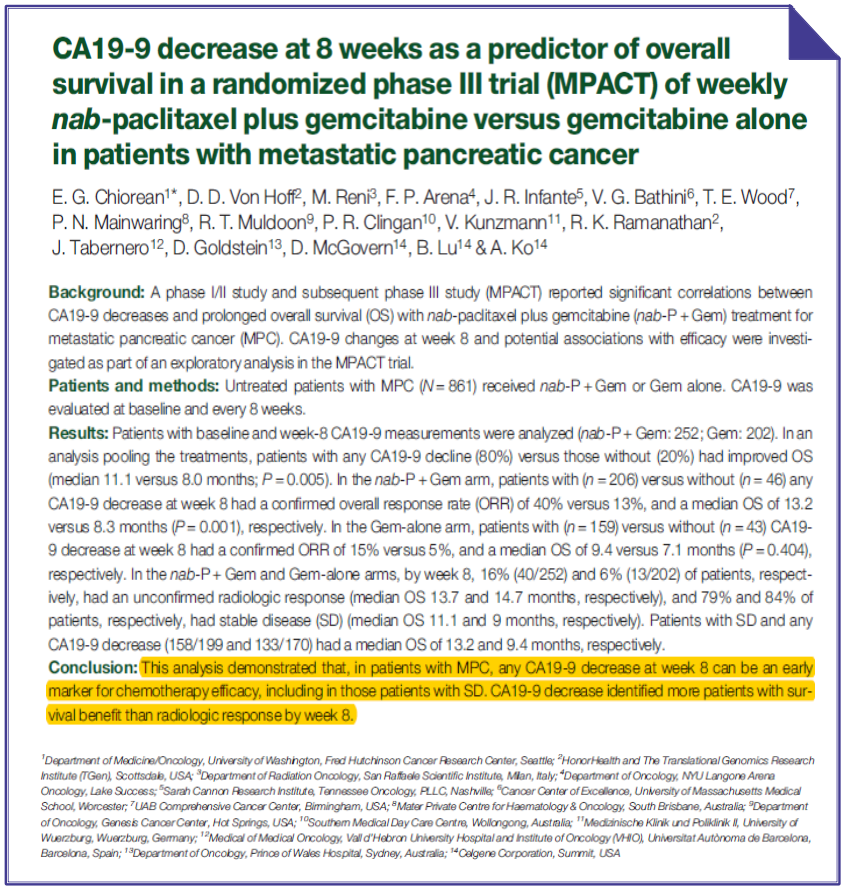
Objective: The objective of this study was to determine the features of carbohydrate antigen (CA) 19-9 decline that correlates best with survival benefit in patients with metastatic pancreatic cancer.

Methods: This is a retrospective study of 225 patients with metastatic pancreatic cancer receiving first-line therapy. Analysis was performed by the Kaplan-Meier method and Cox-proportional hazards ratios. CA 19-9 decline was grouped into quartiles within different CA 19-9 baseline groups. Time to nadir and CA 19-9 decline at month-2 (M2) of therapy were evaluated for patients with a baseline level ≥ 1000 U/mL.

Results: No significant trend in survival was observed across baseline CA 19-9 levels. The greatest survival benefit was seen with a ≥75% decline to nadir. Among those with a ≥75% decline and baseline ≥1000 U/mL, 43 of 57 patients had a >50% decline at M2 of therapy and additional survival benefit was observed with a slower decline to nadir. Small sample sizes limited analysis of other baseline groups. CA 19-9 decline at M2 was not predictive.

Conclusions: In patients with a CA 19-9 ≥1000 U/mL, serial CA 19-9 levels may be considered as a surrogate for serial imaging to evaluate treatment response, with a ≥75% decline indicating the greatest survival benefit. Survival was improved further in the setting of a slower decline to nadir with the highest benefit seen in patients with a nadir occurring at 4 months or longer.

From the *School of Medicine, University of California; †Department of Medicine, Division of Hematology/Oncology, University of California; and ‡UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA.



CA19-9 decrease at 8 weeks as a predictor of overall survival in a randomized phase III trial (MPACT) of weekly *nab*-paclitaxel plus gemcitabine versus gemcitabine alone in patients with metastatic pancreatic cancer

E. G. Chiorean[1]*, D. D. Von Hoff[2], M. Reni[3], F. P. Arena[4], J. R. Infante[5], V. G. Bathini[6], T. E. Wood[7], P. N. Mainwaring[8], R. T. Muldoon[9], P. R. Clingan[10], V. Kunzmann[11], R. K. Ramanathan[2], J. Tabernero[12], D. Goldstein[13], D. McGovern[14], B. Lu[14] & A. Ko[14]

Background: A phase I/II study and subsequent phase III study (MPACT) reported significant correlations between CA19-9 decreases and prolonged overall survival (OS) with *nab*-paclitaxel plus gemcitabine (*nab*-P + Gem) treatment for metastatic pancreatic cancer (MPC). CA19-9 changes at week 8 and potential associations with efficacy were investigated as part of an exploratory analysis in the MPACT trial.

Patients and methods: Untreated patients with MPC ($N = 861$) received *nab*-P + Gem or Gem alone. CA19-9 was evaluated at baseline and every 8 weeks.

Results: Patients with baseline and week-8 CA19-9 measurements were analyzed (*nab*-P + Gem: 252; Gem: 202). In an analysis pooling the treatments, patients with any CA19-9 decline (80%) versus those without (20%) had improved OS (median 11.1 versus 8.0 months; $P = 0.005$). In the *nab*-P + Gem arm, patients with ($n = 206$) versus without ($n = 46$) any CA19-9 decrease at week 8 had a confirmed overall response rate (ORR) of 40% versus 13%, and a median OS of 13.2 versus 8.3 months ($P = 0.001$), respectively. In the Gem-alone arm, patients with ($n = 159$) versus without ($n = 43$) CA19-9 decrease at week 8 had a confirmed ORR of 15% versus 5%, and a median OS of 9.4 versus 7.1 months ($P = 0.404$), respectively. In the *nab*-P + Gem and Gem-alone arms, by week 8, 16% (40/252) and 6% (13/202) of patients, respectively, had an unconfirmed radiologic response (median OS 13.7 and 14.7 months, respectively), and 79% and 84% of patients, respectively, had stable disease (SD) (median OS 11.1 and 9 months, respectively). Patients with SD and any CA19-9 decrease (158/199 and 133/170) had a median OS of 13.2 and 9.4 months, respectively.

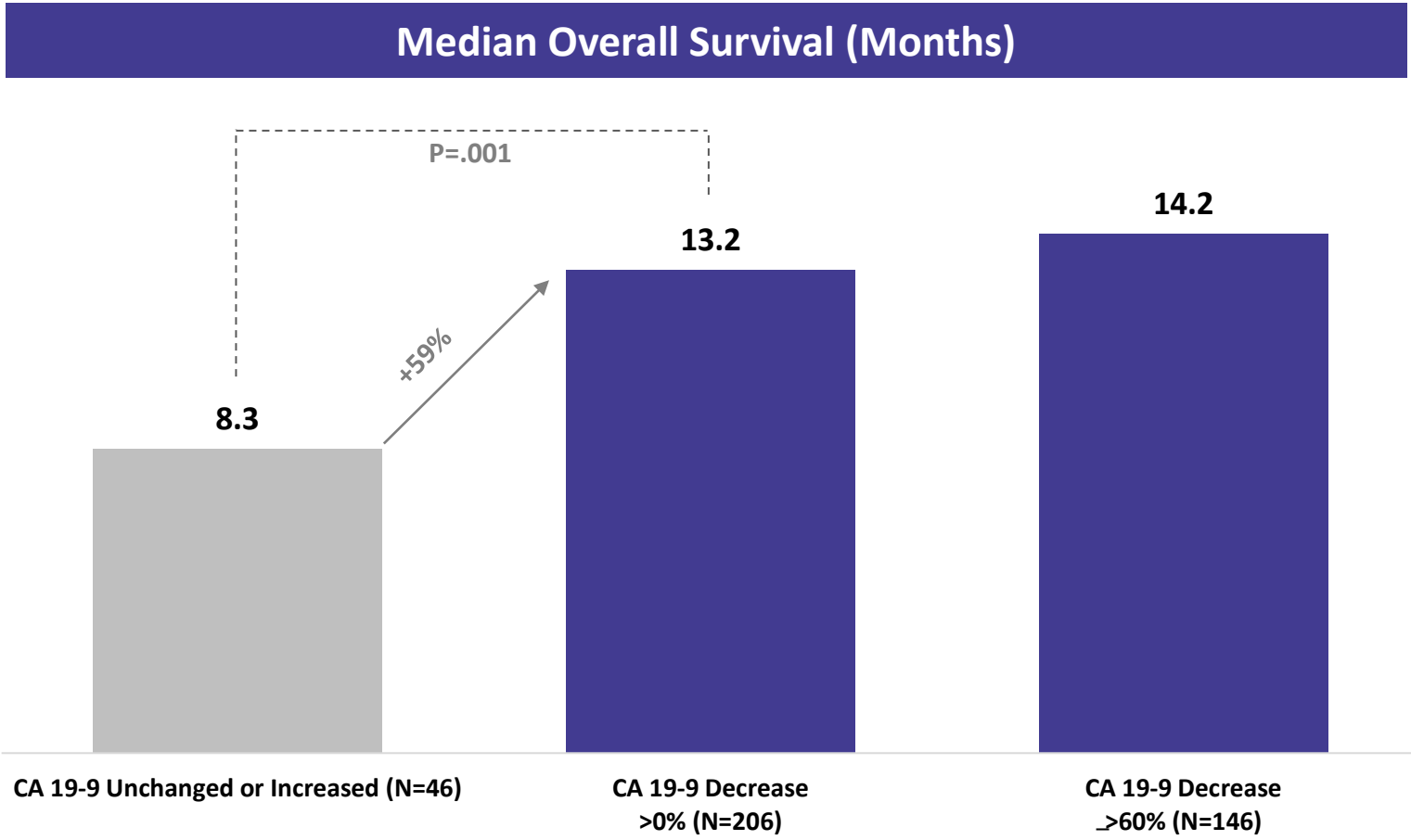
Conclusion: This analysis demonstrated that, in patients with MPC, any CA19-9 decrease at week 8 can be an early marker for chemotherapy efficacy, including in those patients with SD. CA19-9 decrease identified more patients with survival benefit than radiologic response by week 8.

[1]*Department of Medicine/Oncology, University of Washington, Fred Hutchinson Cancer Research Center, Seattle;* [2]*HonorHealth and The Translational Genomics Research Institute (TGen), Scottsdale, USA;* [3]*Department of Radiation Oncology, San Raffaele Scientific Institute, Milan, Italy;* [4]*Department of Oncology, NYU Langone Arena Oncology, Lake Success;* [5]*Sarah Cannon Research Institute, Tennessee Oncology, PLLC, Nashville;* [6]*Cancer Center of Excellence, University of Massachusetts Medical School, Worcester;* [7]*UAB Comprehensive Cancer Center, Birmingham, USA;* [8]*Mater Private Centre for Haematology & Oncology, South Brisbane, Australia;* [9]*Department of Oncology, Genesis Cancer Center, Hot Springs, USA;* [10]*Southern Medical Day Care Centre, Wollongong, Australia;* [11]*Medizinische Klinik und Poliklinik II, University of Wuerzburg, Wuerzburg, Germany;* [12]*Medical of Medical Oncology, Vall d'Hebron University Hospital and Institute of Oncology (VHIO), Universitat Autònoma de Barcelona, Barcelona, Spain;* [13]*Department of Oncology, Prince of Wales Hospital, Sydney, Australia;* [14]*Celgene Corporation, Summit, USA*

Sources: **Diaz Am J Clin Oncol 2019; 42:898-902, Chiorean, E G et al 2016: 654-60 and www.pancan.org*

CA 19-9 Biomarker and Survival Benefit Correlation

- Patients in the MPACT study (Phase III Gem+Nab) whose CA 19-9 levels decreased saw an approximate 5-month incremental median survival benefit (P=.001) compared to patients with unchanged or increased CA 19-9 levels
- Greatest survival benefit observed in patients with CA 19-9 decreases ≥60%

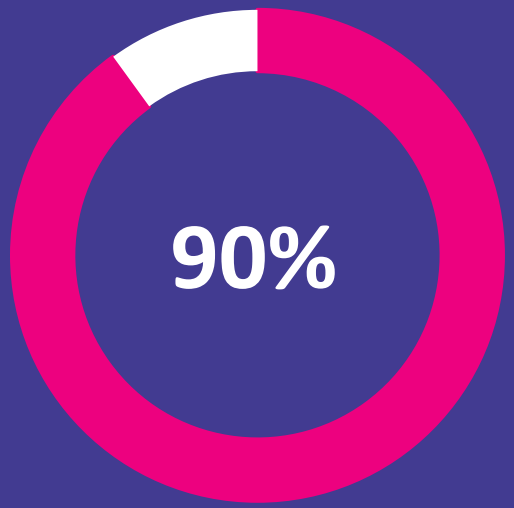


Source: *Chiorean, E G et al 2016: 654-60*

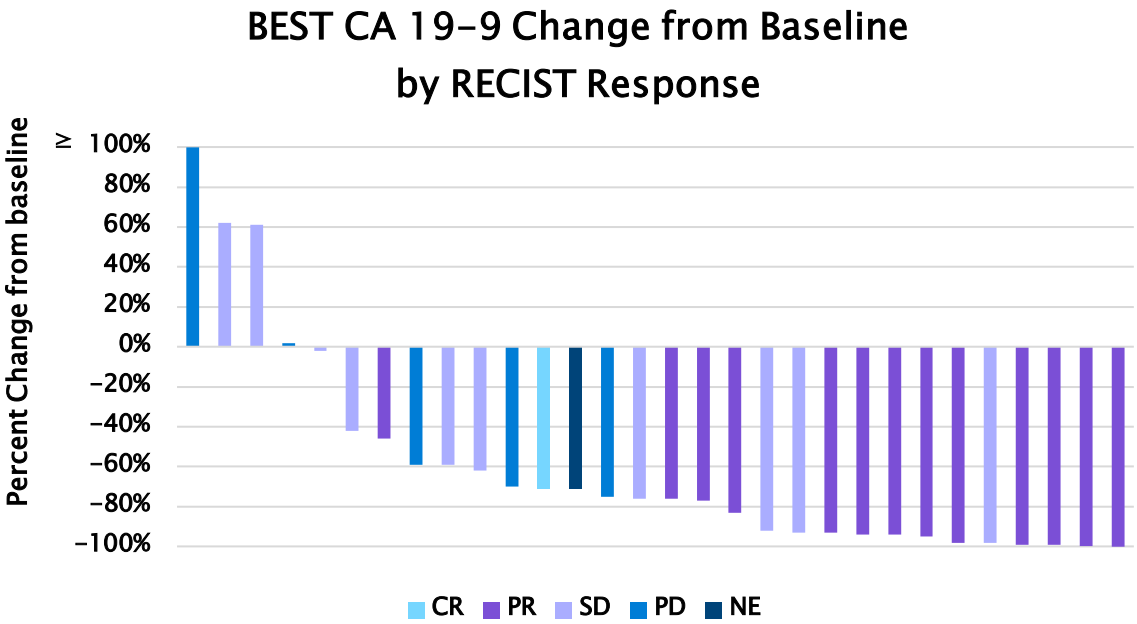
Interim Cohort 4 + P1B CA 19-9 Positive Biomarker Data

CA 19-9 tumor marker often released by pancreatic cancer cells

Patients with CA 19-9 Decrease



- 70% of subjects had a maximum CA 19-9 decrease greater than 60%
- 90% of subjects had a decrease in CA 19-9 levels



ASCO GI Poster Presentation, January, 2022
Best CA 19-9 percent change from Baseline by Response – Cohort 4 + Phase 1b, N=30.
Twenty-one subjects in Cohort 4 + Phase 1b (70%) had a maximum CA 19-9 decrease greater than 60%.

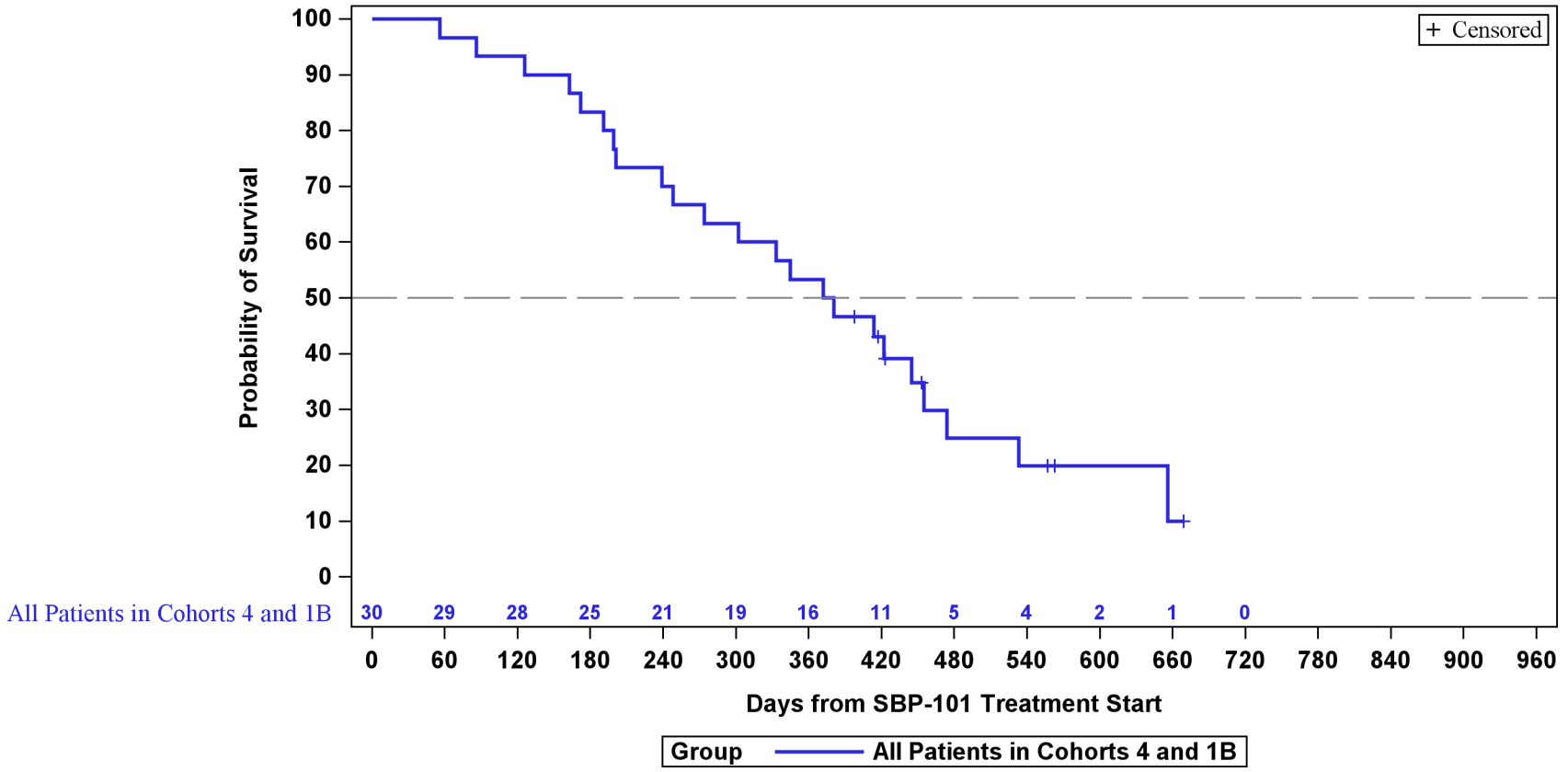
Preliminary Efficacy of SBP-101 + Gemcitabine/Nab-paclitaxel in First-Line Metastatic Pancreatic Ductal Adenocarcinoma

	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%)**	**22/29 (76%)**
Gemcitabine + Nab-paclitaxel (G/A*) n=431**	<1%	23%	27%	20%	**23%**	**48%**

	PFS			OS		
SBP-101 (0.40 mg/kg) + G/A Cohort	Ph1a 2	**Ph1a 4+Ph1b**	G+A*	Ph1a 2	**Ph1a 4+Ph1b**	G+A*
Median (mo)	5.6	**6.0**	5.5	10.3	**12.53*** **	8.5
6 mo (%)	43	**52**	44	100%	**86%**	67%
12 mo (%)	0	**10**	16	43%	**52%**	35%

Data as of 07MAR2022, post ASCO GI Poster Presentation, January, 2022
*G/A = gemcitabine + Nab-paclitaxel
**Historical control data, MPACT study G+A arm, N=431 - Source: Von Hoff NEJM 2013
*** Final Data– Updated post ASCO GI Presentation
Ph1a = Phase 1a
Ph1b = Phase 1b
Disease Control Rate = CR+PR+SD for > 16 weeks

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

Data as of 07MAR2022 - post ASCO GI Poster Presentation, January, 2022
* Maturing data – Not Yet Final

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

Safety Results

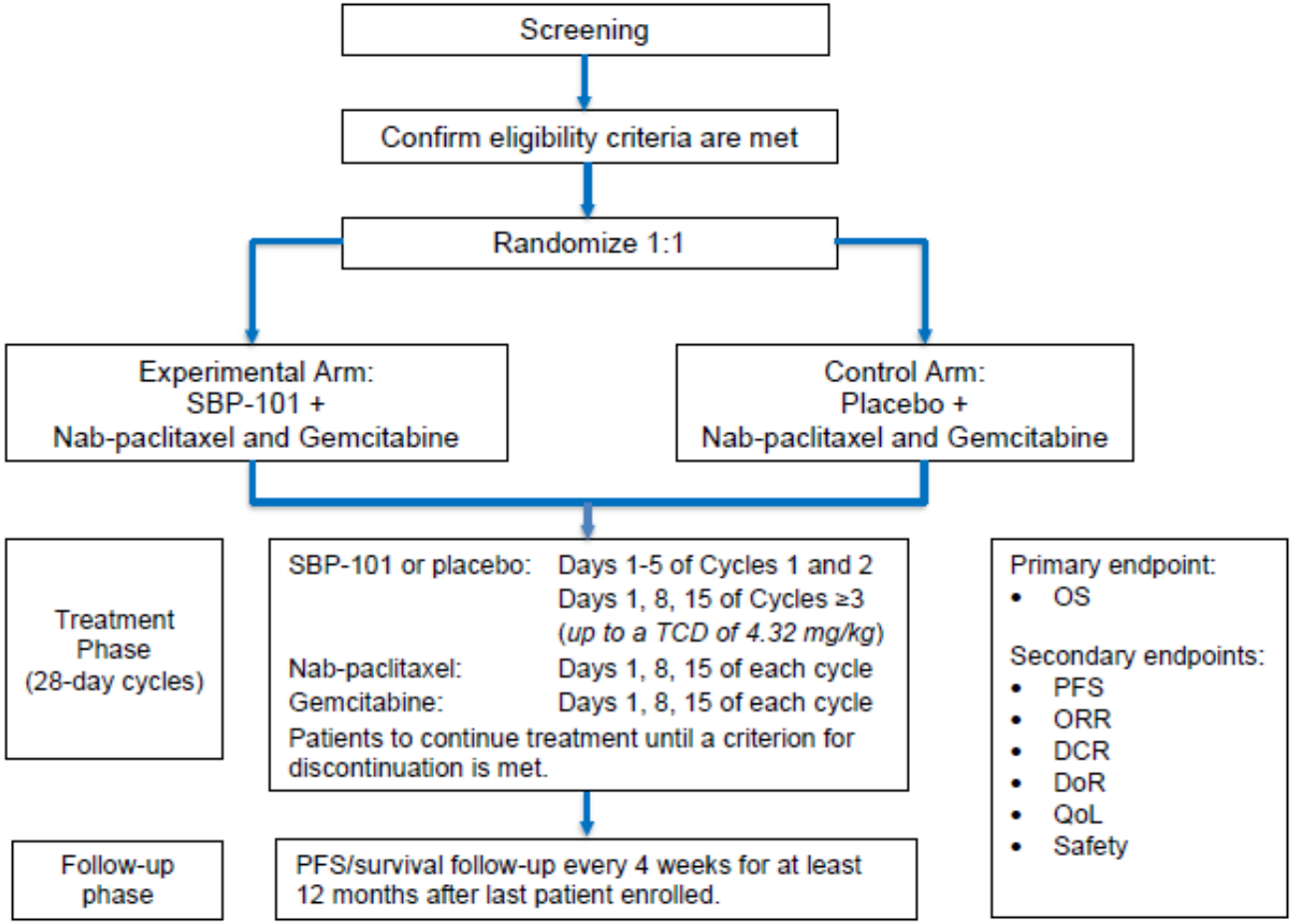
Grade ≥3 AEs of Special Interest	N	SBP-101%		G+A %**
Hematologic Events				
Neutropenia	20	40%		38%
Leukopenia	0	-		31%
Anemia	9	18%		13%
Thrombocytopenia	1	2%		17%
Febrile Neutropenia	1	2%		3%
Non-hematologic Events				
Peripheral Neuropathy	3	6%		17%
Fatigue	6	12%		17%
Diarrhea	6	12%		6%

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%)

ASCO GI Poster Presentation, January 2022
*Historical control data, MPACT study, G+A arm, N= 431 - Source: Von Hoff 2013
** G/A = gemcitabine + Nab-paclitaxel

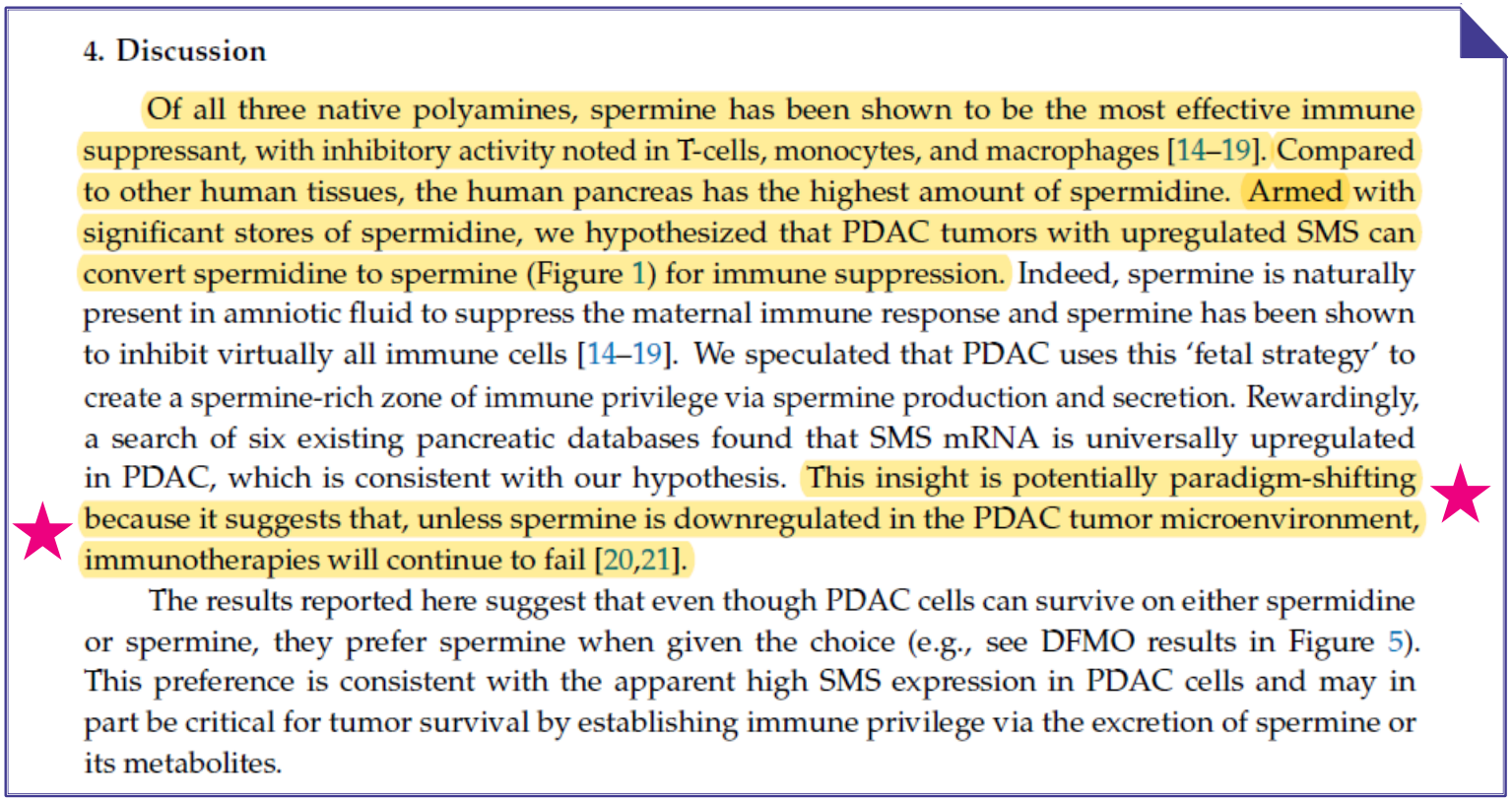
Phase 2/3 Pancreatic Cancer Trial in Subjects Previously Untreated for Metastatic Pancreatic Ductal Adenocarcinoma

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



Area of Future Exploration: SBP-101 Combined with IOs

- Historical clinical trials using IO agents have been unsuccessful
- A potential hypothesis is that excess polyamines, especially spermine, insulate the tumor microenvironment from immune cells
- SBP-101 is a *synthetic analogue* of spermine, which is believed to reduce endogenous polyamine production



4. Discussion

Of all three native polyamines, spermine has been shown to be the most effective immune suppressant, with inhibitory activity noted in T-cells, monocytes, and macrophages [14–19]. Compared to other human tissues, the human pancreas has the highest amount of spermidine. Armed with significant stores of spermidine, we hypothesized that PDAC tumors with upregulated SMS can convert spermidine to spermine (Figure 1) for immune suppression. Indeed, spermine is naturally present in amniotic fluid to suppress the maternal immune response and spermine has been shown to inhibit virtually all immune cells [14–19]. We speculated that PDAC uses this 'fetal strategy' to create a spermine-rich zone of immune privilege via spermine production and secretion. Rewardingly, a search of six existing pancreatic databases found that SMS mRNA is universally upregulated in PDAC, which is consistent with our hypothesis. This insight is potentially paradigm-shifting because it suggests that, unless spermine is downregulated in the PDAC tumor microenvironment, immunotherapies will continue to fail [20,21].

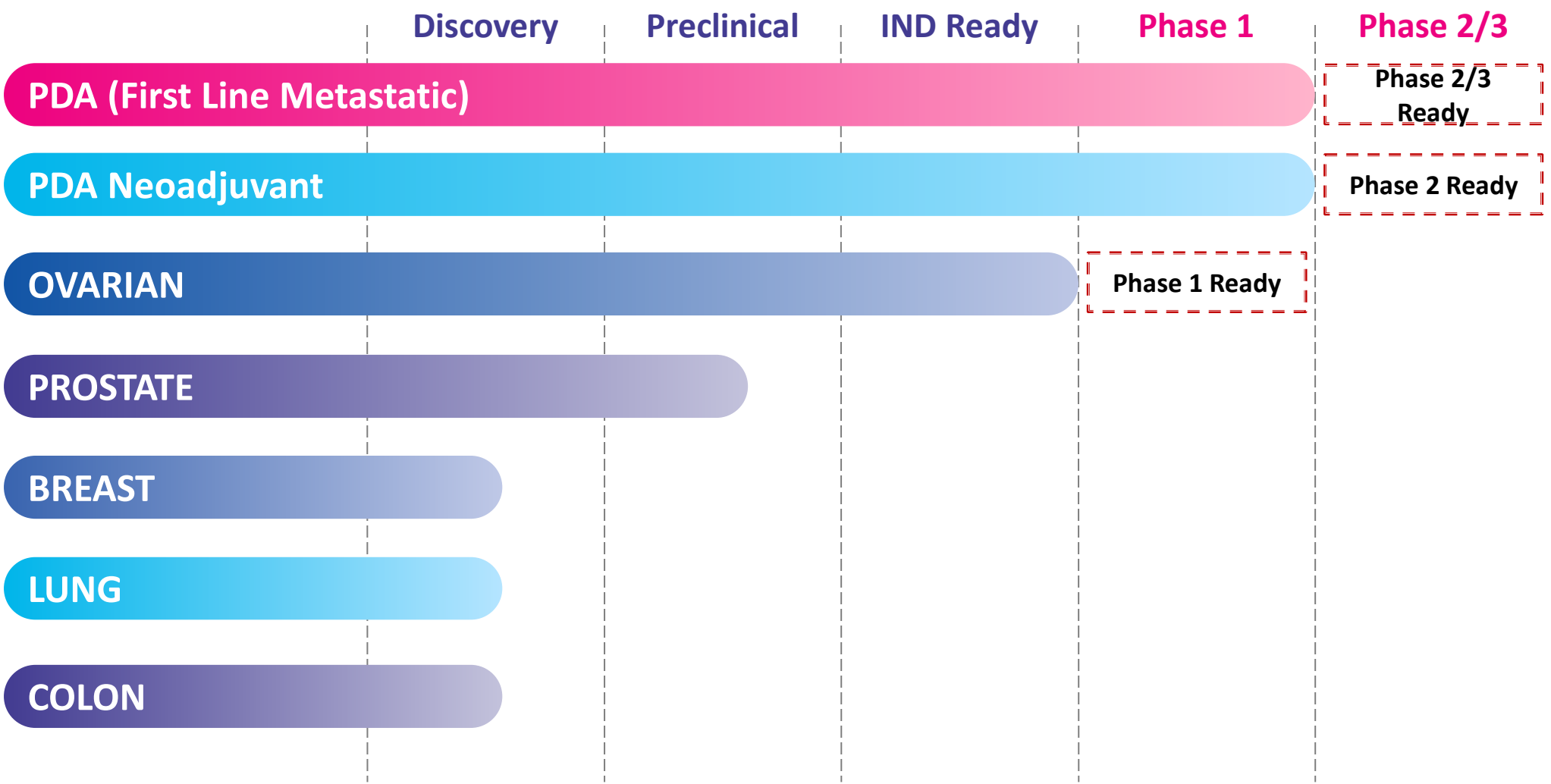
The results reported here suggest that even though PDAC cells can survive on either spermidine or spermine, they prefer spermine when given the choice (e.g., see DFMO results in Figure 5). This preference is consistent with the apparent high SMS expression in PDAC cells and may in part be critical for tumor survival by establishing immune privilege via the excretion of spermine or its metabolites.

Potential for SBP-101 to recondition tumor microenvironment and act as sensitizing agent for IOs

Source: *Massaro et al. "Investigation of Polyamine Metabolism and Homeostasis in Pancreatic Cancers." Med. Sci. 2017, 5, 32; doi:10.3390/medsci5040032*

Significant SBP-101 Polyamine Metabolic Inhibitor Pipeline Expansion Opportunity

Upregulated polyamine metabolism is also a phenotypic change caused by certain oncogenic mutations, creating potential for future patient stratification strategies in other cancers



Cash Balance and Capitalization

Cash Balance as of September 30, 2021	$14,072,000

Capitalization Table	
Common Stock Outstanding as of September 30, 2021	13,434,152
Stock Options @ $5.87 WAEP	2,489,136
Restricted Stock Units Outstanding	16,185
Warrants @ $4.59 WAEP	5,109,501
Common stock outstanding and reserved for as of September 30, 2021	**21,048,974**

Milestones

2022

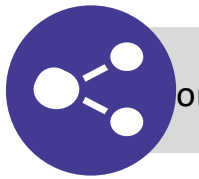
- ASCO GI Poster Presentation (1Q – January)
- First Patient Enrolled in randomized phase 2 study (1Q’22)
- Final Data from phase 1 trial (1H'22)
- Initiate Ovarian Cancer Clinical Program (1H’22)
- Close Merger Transaction (1H’22)
- Initiate Neoadjuvant Pancreatic Trial (2H'22)

SBP-101 Summary

Unique dual-attack MOA is synergistic with other agents, potentially enhancing anti-tumor response

Favorable safety & tolerability profile and subcutaneous administration in clinical studies to date supports potential ease of use

Interim data from Phase 1a/1b trial presented at ASCO GI January 2022; final data 1H ‘22



Encouraging interim efficacy and tumor marker signals
onsistent with preferential uptake of SBP-101 in tumor cells lending to initiation of randomized trial in 1L metastatic Pancreatic Cancer

Expansion to Ovarian Cancer and the potential to expand SBP-101 into other cancers with known elevated levels of polyamines

Advancing SBP-101 clinical development to create significant stockholder value