TEMPEST

THERAPEUTICS

Company Overview

July 2022

Information Regarding Disclosures

Forward-Looking Statements

This presentation contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (the "Securities Act")) concerning Tempest Therapeutics, Inc. ("Tempest Therapeutics"). These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Tempest Therapeutics, as well as assumptions made by, and information currently available to, management of Tempest Therapeutics. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "could", "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," and other similar expressions. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: our strategies, prospects, plans, expectations or objectives for future operations; the progress, scope or timing of the development of our product candidates; the benefits that may be derived from any future products or the commercial or market opportunity with respect to any of our future products; our ability to protect our intellectual property rights; our anticipated operations, financial position, ability to raise capital to fund operations, revenues, costs or expenses; statements regarding future economic conditions or performance; statements of belief and any statement of assumptions underlying any of the foregoing. Many of these risks are described in greater detail in the Form 10-Q filed by Tempest Therapeutics with the Securities and Exchange Commission on May 13, 2022.

Except as required by applicable law, Tempest Therapeutics undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

Introduction to Tempest Therapeutics

A diversified, novel portfolio designed to deliver meaningful therapies to cancer patients

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Products — First-in-class, orally available molecules with clinical benefit observed in initial studies*

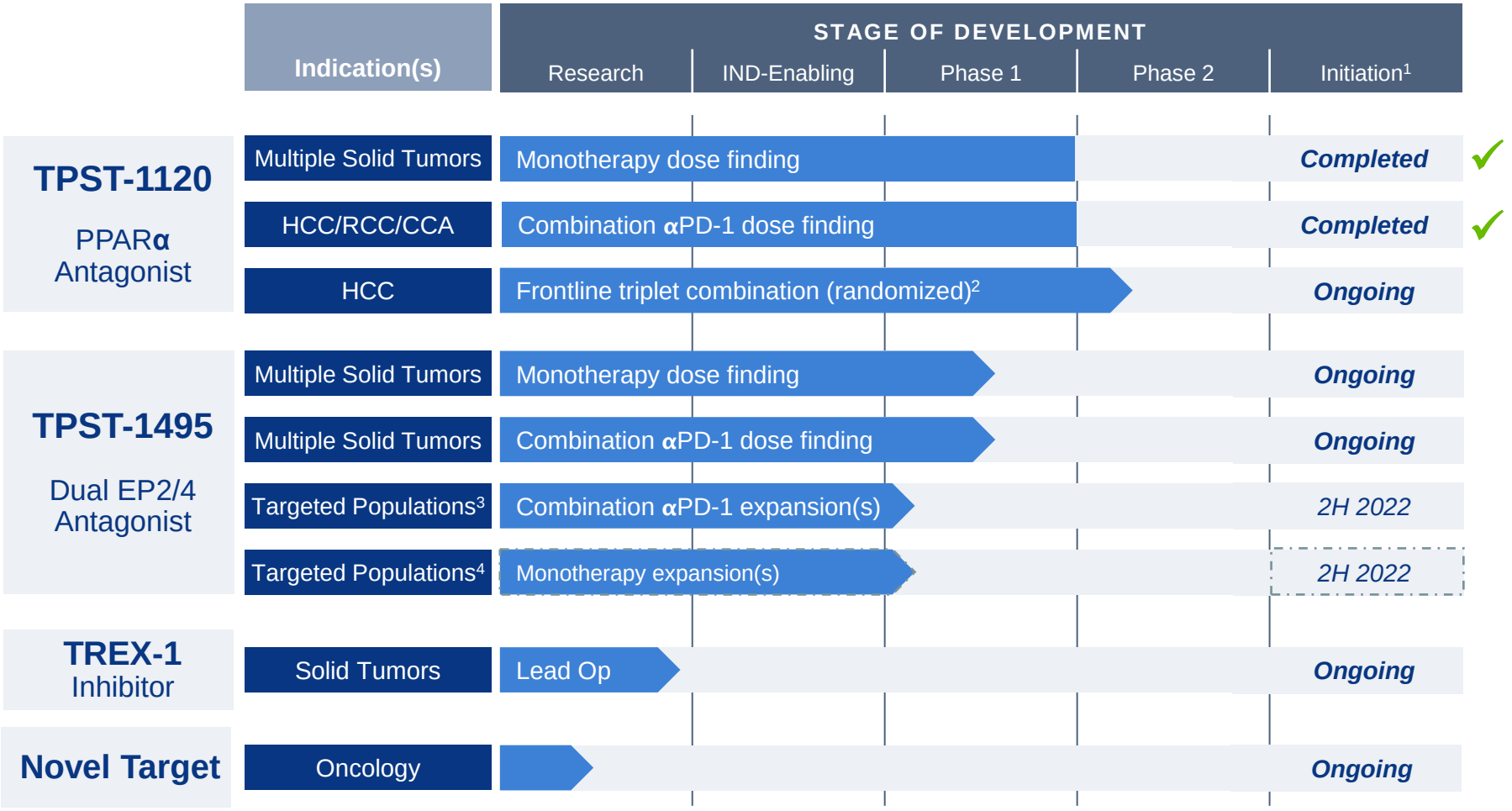
Strategy — Pursuing solid tumor therapies with potential for substantial impact

Team — Experienced management with track record of delivering value

Catalysts — Financed into the second half of 2023, through potentially catalytic news flow

* "First-in-class if approved by the FDA. Benefit observed in first clinical program, TPST-1120, and reported in an oral presentation at ASCO 2022

First-in-Class* Oncology Pipeline with Broad Potential



"HCC" hepatocellular carcinoma, "RCC" renal cell carcinoma, "CCA" cholangiocarcinoma

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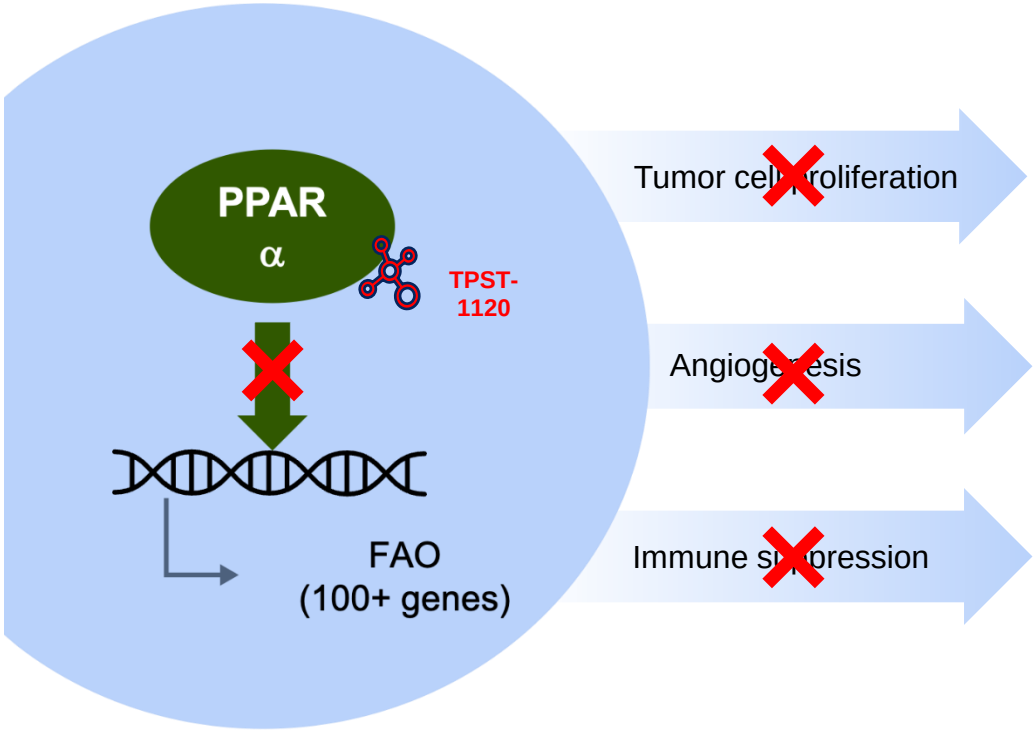
* If approved by FDA [1] Timing is an estimate based on current projections. [2]Pursuant to a collaboration with Roche; TPST retains all product rights. [3] Study could be either a single indication or biomarker-based basket [4] With additional funding, monotherapy expansion(s) would be in select indications based on target expression and/or a biomarker-positive basket cohort;

TPST-1120

First-in-Class PPARα Antagonist

TPST-1120: First-in-Class PPARα Antagonist

Targets both tumor cells and immune suppressive cells

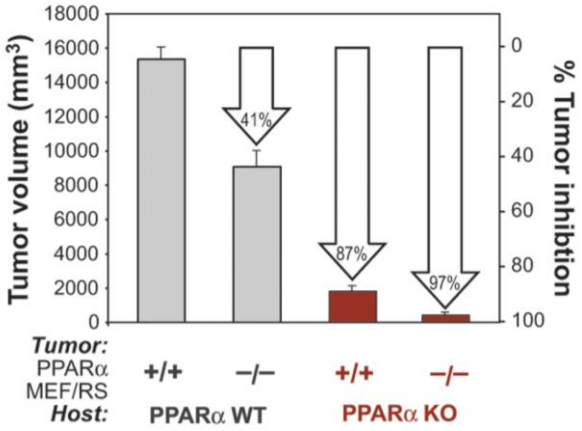


- **FAO** is a key cancer metabolic adaptation that supports tumor growth and metastasis
- **FAO** is a principal metabolic pathway for immune suppressive cell types and FAO induces angiogenesis
- **PPARα** is a transcription factor and master regulator of FAO, controlling > 100 lipid metabolism genes
- **Inhibiting PPARα** to reduce FAO is a promising strategy to inhibit tumor growth and relieve immunosuppression.

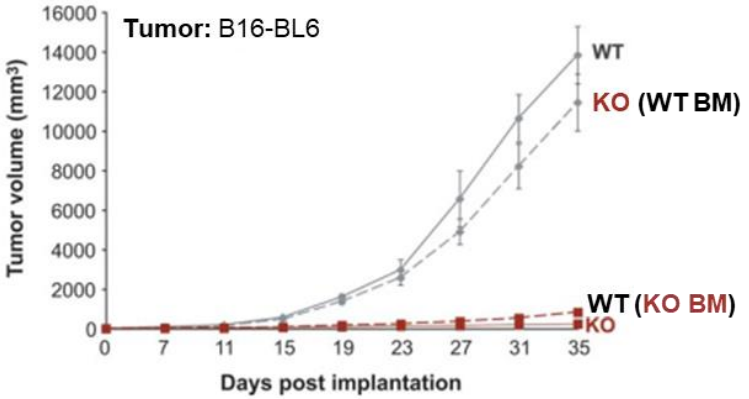
Genetic Validation for Targeting PPARα

PPARα and FAO are required to sustain tumor growth

PPARα KO Prevents Tumor Growth

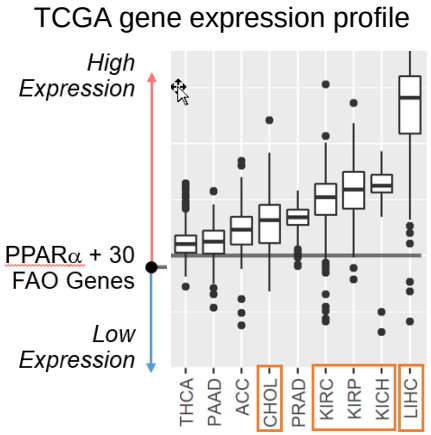


PPARα Signaling in Immune Cells is Critical For Tumor Growth



Bone Marrow Transplantation Confers Transplant Phenotype

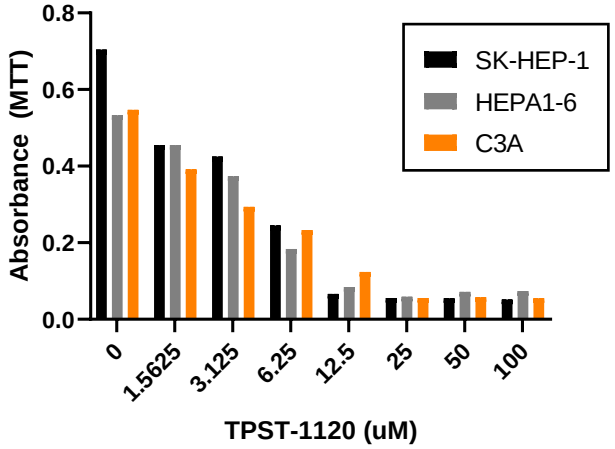
FAO-dependent tumor analysis informs clinical development strategy



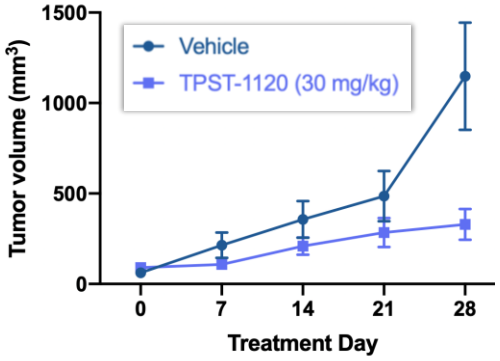
Kaipainen et al., PLoS ONE 2007, 2(2): e260

TPST-1120 MOA:
Combined Tumor Cell Killing and Immune Activation

Direct Tumor Killing

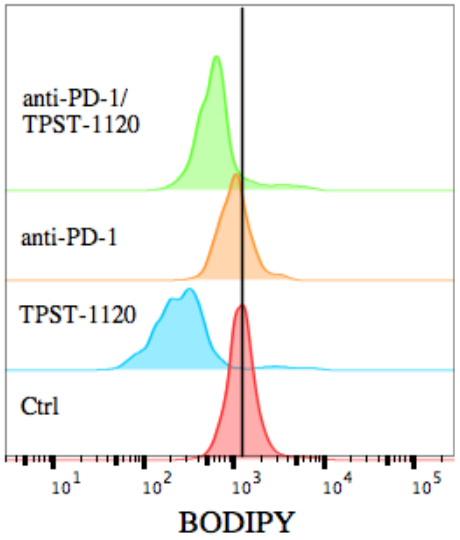


Caki-1 RCC Xenograft model

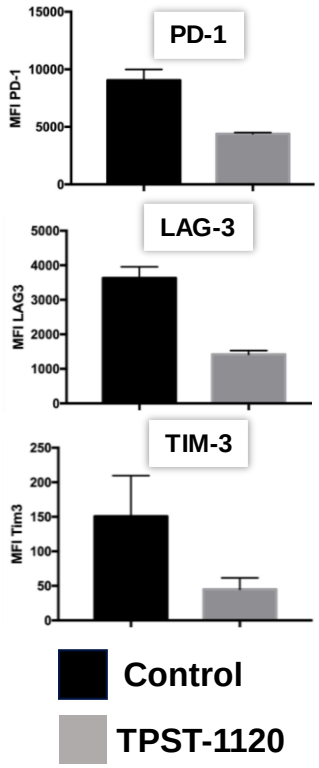


Immune Activation in the TME

Dendritic cells
(CD45$^+$CD11c$^+$F4/80$^-$)



CD8$^+$ T cells



β-catenin Pathway as a Potential Biomarker

Frequently Activated in HCC and is PPARα- and FAO-Dependent

- Wnt/β-catenin pathway is critical for cellular functions including stem cell regeneration, organogenesis and tumorigenesis (i.e., EMT)
- PPARα is a direct target of β-catenin in HCC
  - PPARα expression is higher in CTNNB1-mutated human HCC
- Activation of WNT/β-catenin pathway occurs frequently in HCC: 40-70%[1,2,3]
- β-catenin pathway augmentation can occur through multiple mechanisms[1,2,3]
- β-catenin activated HCC is PPARα dependent
  - PPARα KO sufficient to prevent HCC initiation and progression ($Apc^{hep-/-}$ and $JNK1/2^{-/-}$ mice) [4,5]
  - PPARα-induced FAO in $Apc^{hep-/-}$ mice is the driving force for energy production in tumor
- Available genetic tests for CTNNB1, APC and modulators of β-catenin pathway

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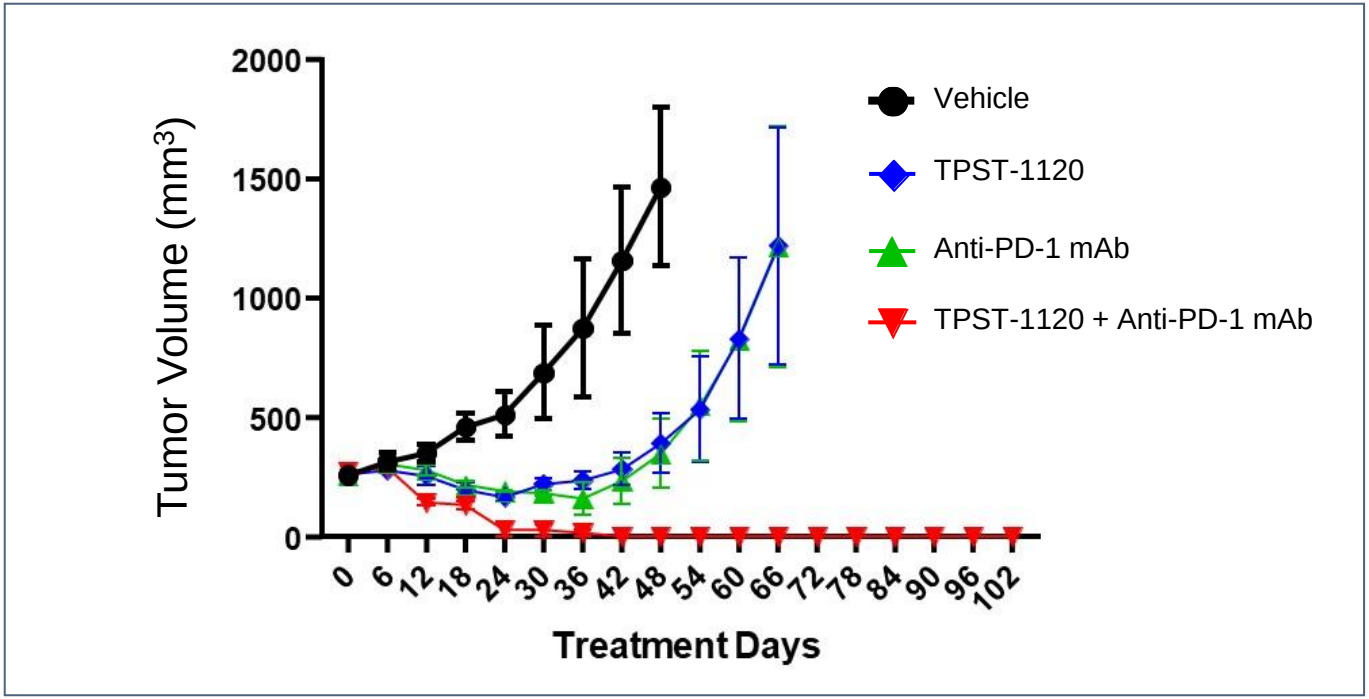
(1) Gao et al. Cell 2019;179(2):561-577 (2) TCGA. Cell 2017;169(7):1327-1341 (3) Wang et al Cancers 2019; 11: 926-946 (4) Senni et al. Gut 2019;68:322-334 (5) Manieri et al PNAS 2020 doi/10.1073/pnas.2002672117

Preclinical HCC Data Support Clinical Development Strategy

Complete and durable tumor cures with TPST-1120 + αPD-1 therapy

Syngeneic β-Catenin-driven hepatocellular carcinoma model*



Explanation for synergy | PD-L1 / PD-1 ligation induces FAO in T cells (*Patsoukis et al. Nat. Comm (2015)*

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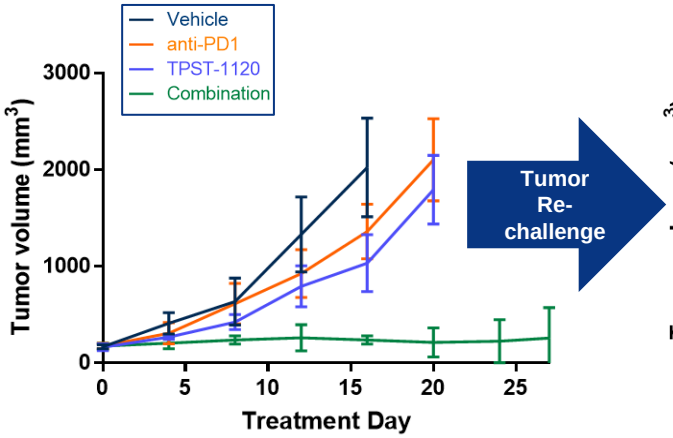
*Hepa 1-6 tumor cells are β-catenin driven (Pandit et al. BMC Cancer (2018) 18:783)
Source: Dipak Panigrahy collaboration; Rx initiated 12d post implantation; TPST-1120 30 MGPK BID; α-PD-1 200 ug Q3d

TPST-1120 + α-PD-1 Synergize and Confer Durable Immunity

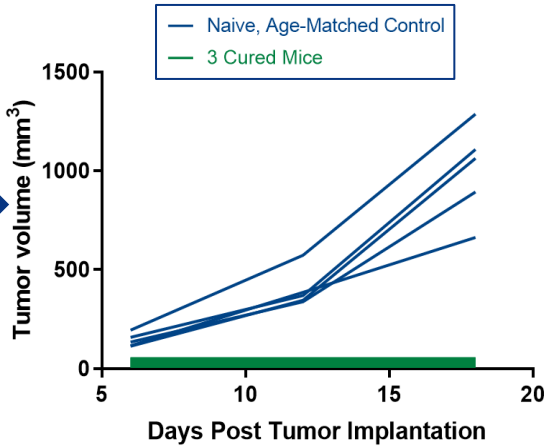
MC38 colorectal cancer tumor model, C57BL/6 immunocompetent mice

TPST-1120 + anti-PD1 treatment

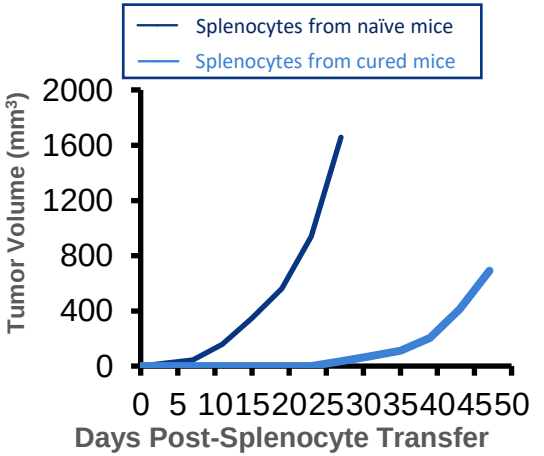


C57BL/6 mice bearing 150 mm³ MC38 flank tumors treated with TPST-1120 30 mg/kg BID and 200 µg α-PD-1 Q3D

Tumor re-challenge



Adoptive transfer of splenocytes into naïve C57BL/6 mice, MC38 tumor cell challenge



Adoptive transfer of splenocytes from naïve C57BL/6 mice or MC38 tumor-bearing mice cured with TPST + αPD-1 into naïve C57BL/6 mice, followed by challenge with 1 x 10⁶ MC38 tumor cells

Anti-Tumor Activity Observed in TPST-1120 Phase 1 Study

RECIST responses observed in IO-refractory patients and IO-resistant indications

Monotherapy
3+3 Design
TPST-1120 up to 600 mg BID

Combo with αPD-1 (nivo)
3+3 Design
TPST-1120 up to 600 mg BID
Full-dose nivolumab

RP2D = 600mg BID for both mono & combo

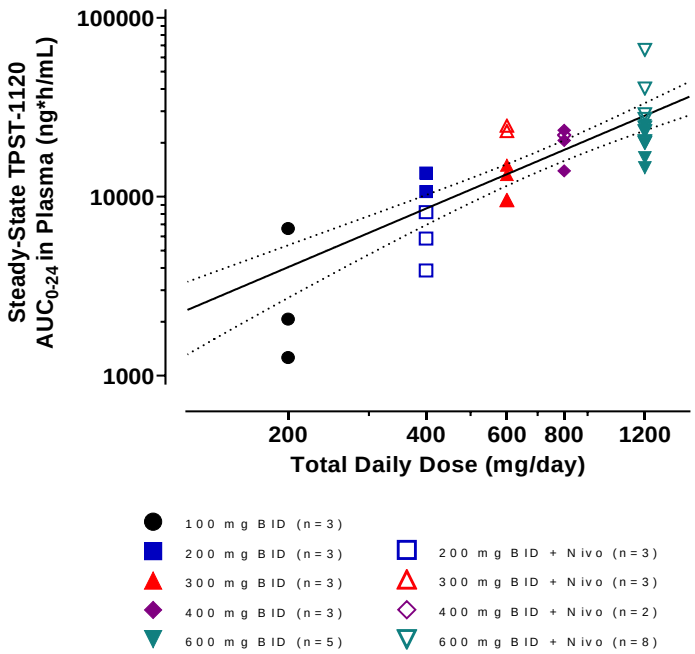
- RECIST responses and prolonged SD in late-stage patients with difficult-to-treat indications[1]
  - 30% ORR at two highest dose cohorts in combination with nivolumab
    - Responding patients were either refractory to IO or had an IO-non-responsive indication
    - Apparent dose response
  - 53% DCR with monotherapy in late-stage patients with difficult indications
- Dose-proportional exposure
- Low-grade toxicity profile
- Frontline randomized HCC study ongoing

1. Oral presentation at ASCO 2022

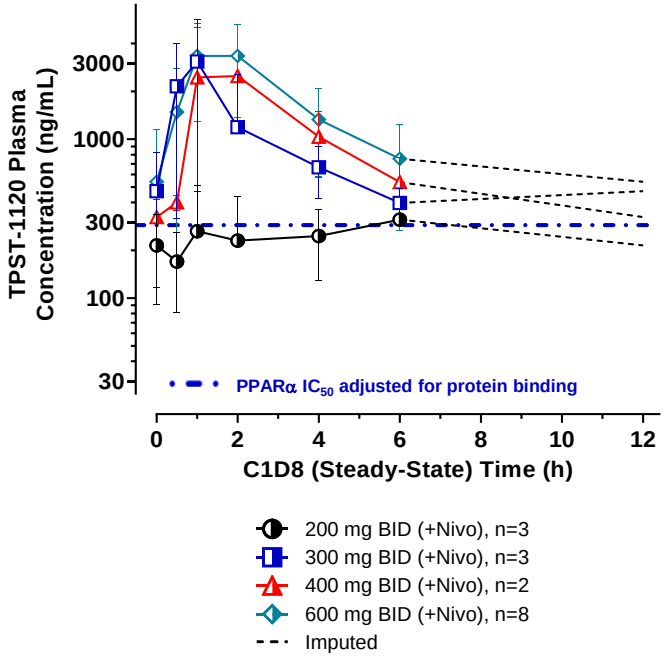
TPST-1120 Exposure Increases Linearly with Dose

Pharmacokinetics

Dose-Exposure Relationship



Steady-State Profile (Combination)



TPST-1120 Has A Tolerable Safety Profile

Treatment-related adverse events occurring in ≥ 2 Patients

AE, n (%)	TPST-1120 Monotherapy (N=20)	
	Any Grade	Grade 3
Any AE	10 (50.0)	1 (5.0)†
Nausea	4 (20.0)	0
Fatigue	3 (15.0)	0
Diarrhoea	2 (10.0)	0

†Hypertension

AE, n (%)	TPST-1120 + Nivolumab (N=18)	
	Any Grade	Grade 3
Any AE*	15 (83.3)	3 (16.7)^
Fatigue	6 (33.3)	0
Diarrhoea	4 (22.2)	0
Nausea	3 (16.7)	0
Abdominal pain	2 (11.1)	0

^Arthralgia, Hepatic enzymes increased, Muscle spasms

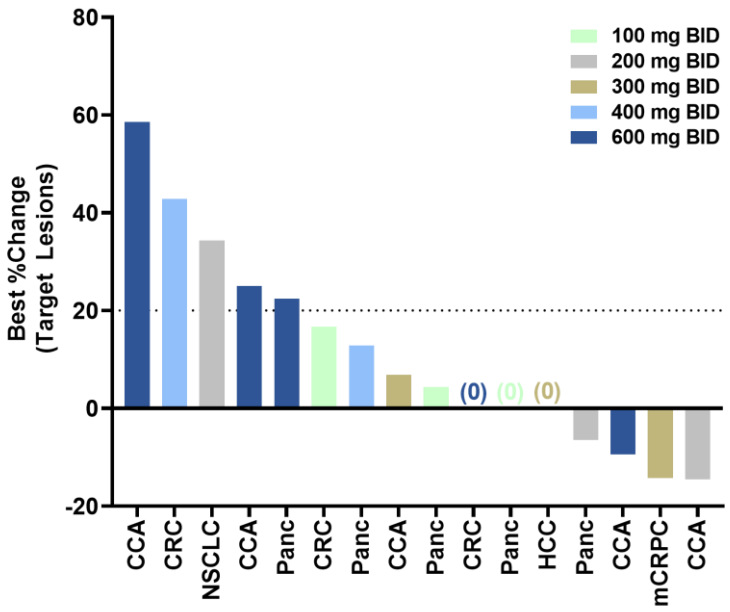
*Related to either TPST-1120 or nivolumab

- TPST-1120 showed tolerable safety profile as monotherapy and in combination with nivolumab
- Most common treatment related AEs were nausea, fatigue and diarrhea
- No DLTs during dose escalation
- RP2D 600 mg PO BID for monotherapy and combination

TPST-1120 Clinical Benefit Observed in Late-Stage Patients

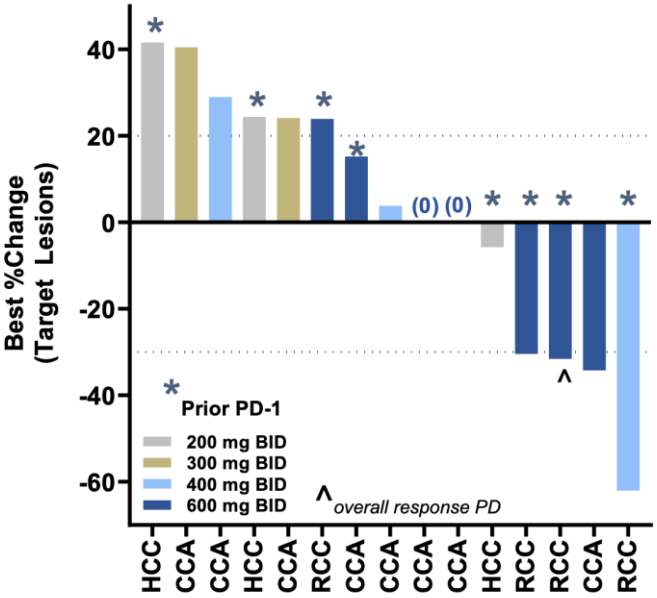
RECIST responses and disease control in difficult-to-treat patient population

Monotherapy (N=19): 53% DCR



- Prolonged disease control and tumor shrinkage in late line patients (4th)[1]
- Difficult-to-treat indications, e.g., CRC, pancreatic and cholangiocarcinoma

Combination with Nivolumab (N=15): 20% ORR



- Responses in patients with IO refractory (RCC) or IO non-responsive (CCA) indications
- All patients with approved PD1
- Responses in two highest dose cohorts

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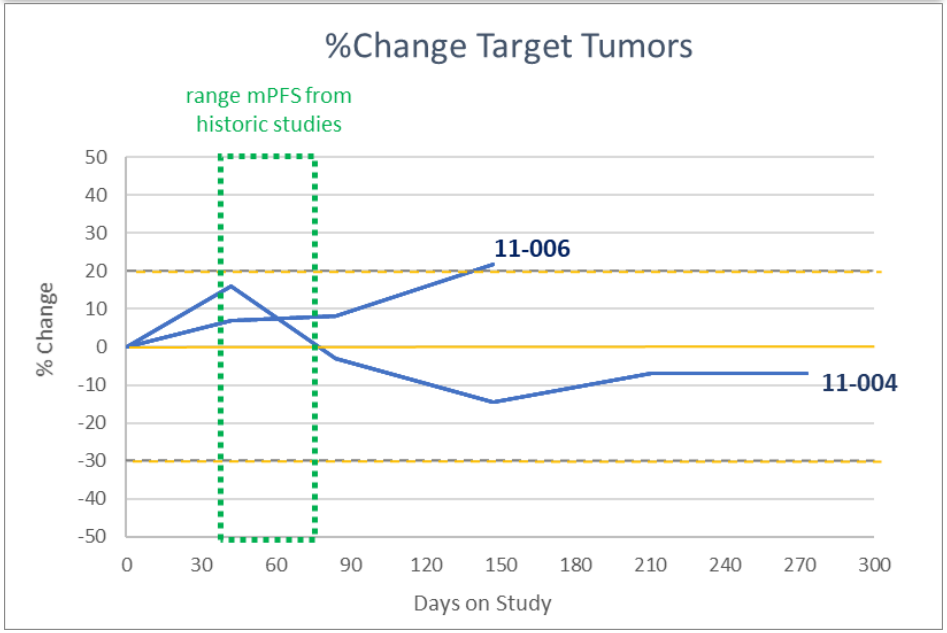
Response evaluable patients include pts with a postbaseline scan or discontinued treatment due to disease progression. DCR, disease control rate = complete response + partial response + stable disease. April 15, 2022 data cut.

[1] Median three prior lines of therapy

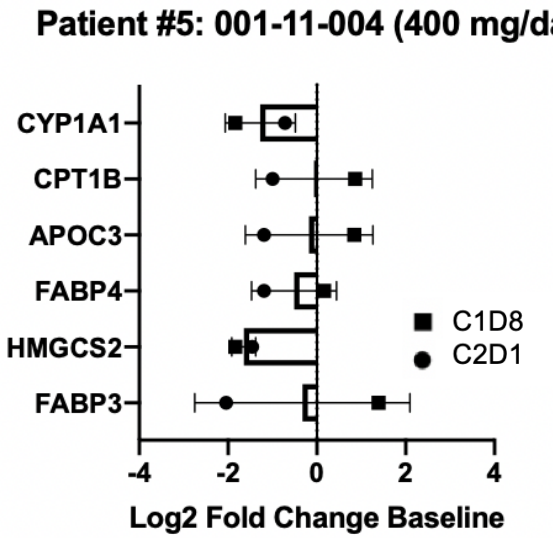
Monotherapy Tumor Control in Late-Line Cholangiocarcinoma

Clinical benefit associated with TPST-1120 target engagement

Long-term stable disease in two advanced CCA patients*



Decreased PPARα target genes in Patient 11-004



- *CYP1A1 extrahepatic fatty acid metabolism*
- *CPT1B regulatory site for fatty acid oxidation on mitochondria*
- *APOC3 regulates triglyceride metabolism*
- *FABP4 (Fatty acid-binding protein 4)-fatty acid uptake*
- *HMGCS2 ketone body metabolism, responds during fasting*
- *FABP5 (Fatty acid-binding protein 5)-fatty acid uptake & transport*

*Both subjects had IDH1 mutation

Data as of Sept 10, 2021, database not 100% monitored

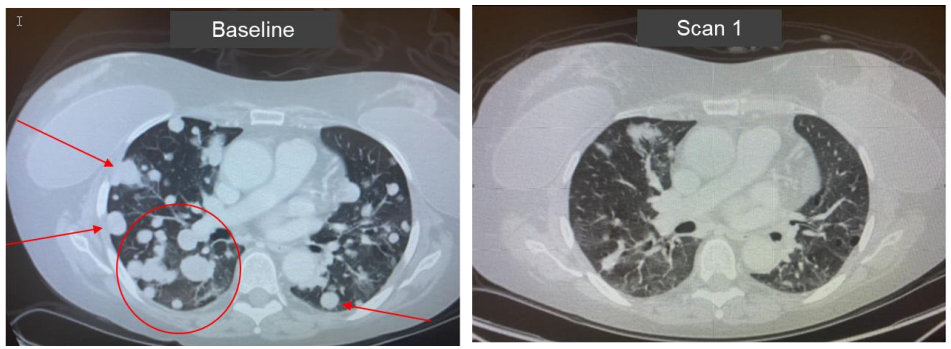
RCC Responses with TPST-1120 + Nivolumab

Two of two patients with IO-refractory, late-line, RCC experienced rapid RECIST responses

Subject 14-008

- 1st scan -54% RECIST response with 12+ month ongoing duration (current response -62%)
- Prior therapy (best response, reason for discontinuation)
  - 1L: ipilimumab + nivolumab (SD, PD)
  - 2L: cabozantinib (SD, PD)
  - 3L: everolimus (SD, PD)
- Sites of metastatic disease: pulmonary; multiple soft tissue (chest, peri-renal, peri-vaginal); bone

-54% at 1st Scan



Subject 22-008

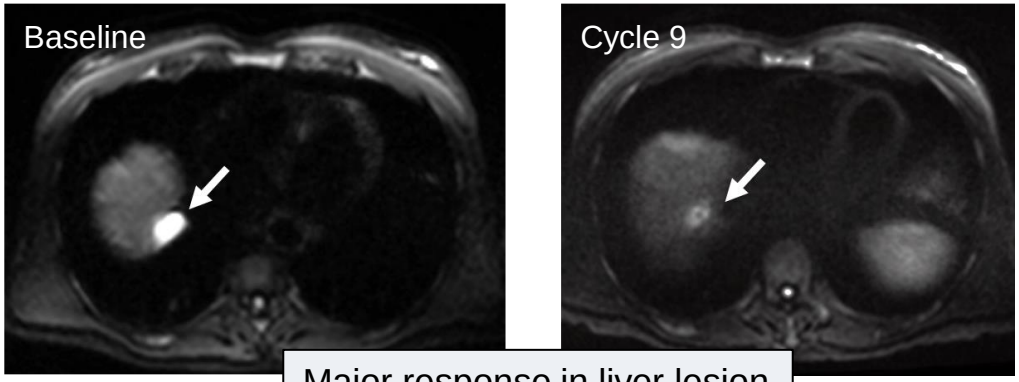
- Extensive lymphadenopathy in chest and abdomen, nephrectomy bed recurrence, malignant pericardial effusion
- LDH 2X ULN
- Prior therapy (best response, reason for discontinuation)
  - 1L: pembrolizumab + axitinib (SD, PD)
  - 2L: cabozantinib (SD, PD)
- Rapid -30% RECIST response on study, but came off treatment for unrelated AE[1]

Consistent with preclinical data showing that TPST-1120 reverses T cell exhaustion

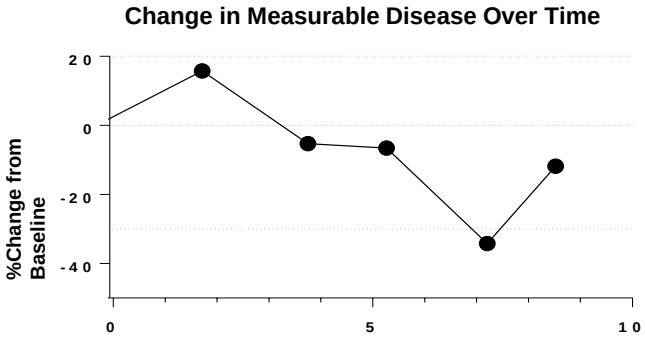
[1] Was unable to restart treatment; disease progressed while off treatment

Cholangiocarcinoma Response with TPST-1120 + Nivolumab

Patient with late line PD-L1 negative and MSS metastatic cholangiocarcinoma



Major response in liver lesion

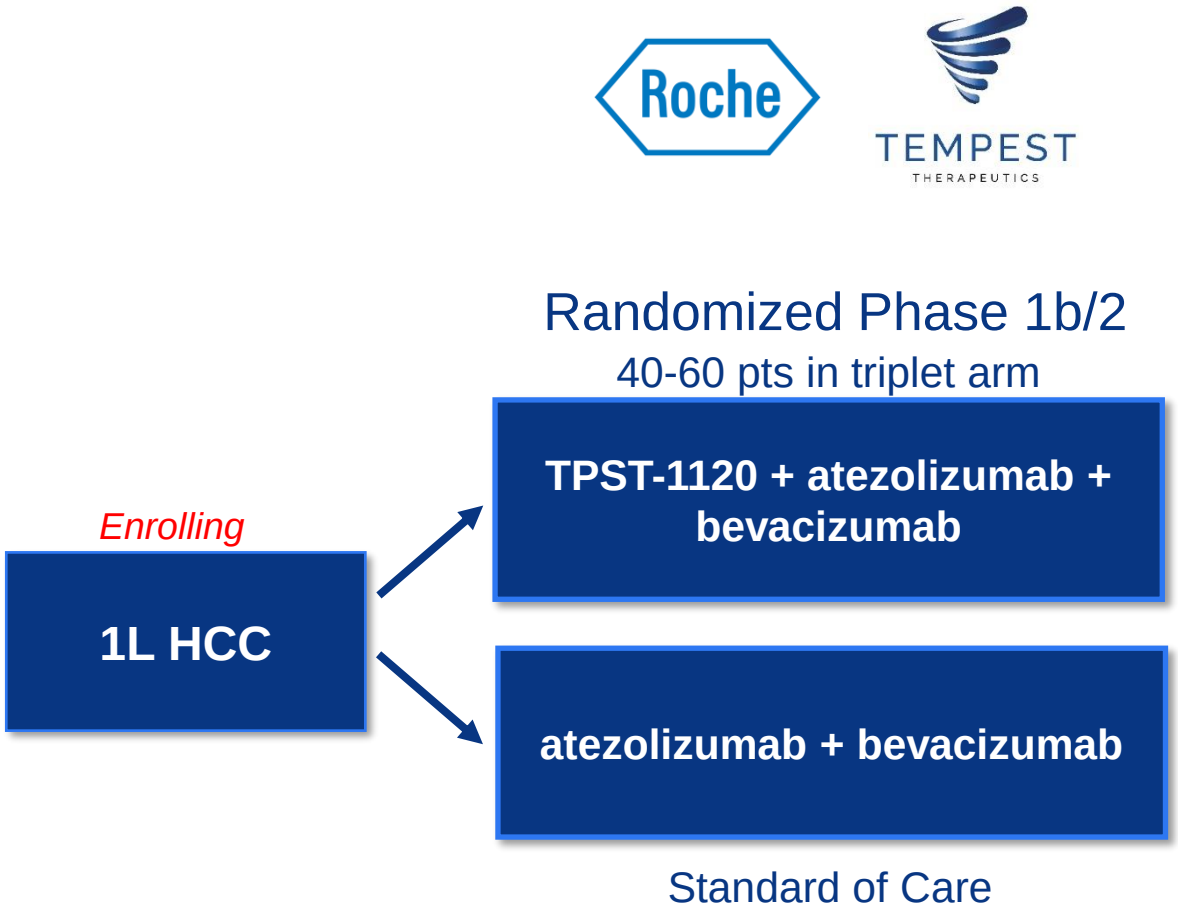


Baseline SLD: ***76 mm***
Target lesion sites: ***liver, lymph node, peritoneum***

Treatment History

	Prior Regimen	Reason for DC
1	Gemcitabine	Adjuvant therapy
2	Gem + Cisplatin + Herception	Completed
3	Capectabine + RT	Completed
4	Herceptin	Progressive Disease
5	Gem + Herceptin	Progressive Disease
6	FOLFOX	Progressive Disease

TPST-1120 Accelerating to Frontline HCC Randomized Study



- Standard of care 1L regimen +/- TPST-1120
- Ongoing multi-arm global study[1]
  - US, Asia, Europe
- Roche operationalizing
- ORR for first 40 subjects anticipated by YE22/early 2023

[1] Morpheus HCC study allows for rapid implementation (NCT04524871)

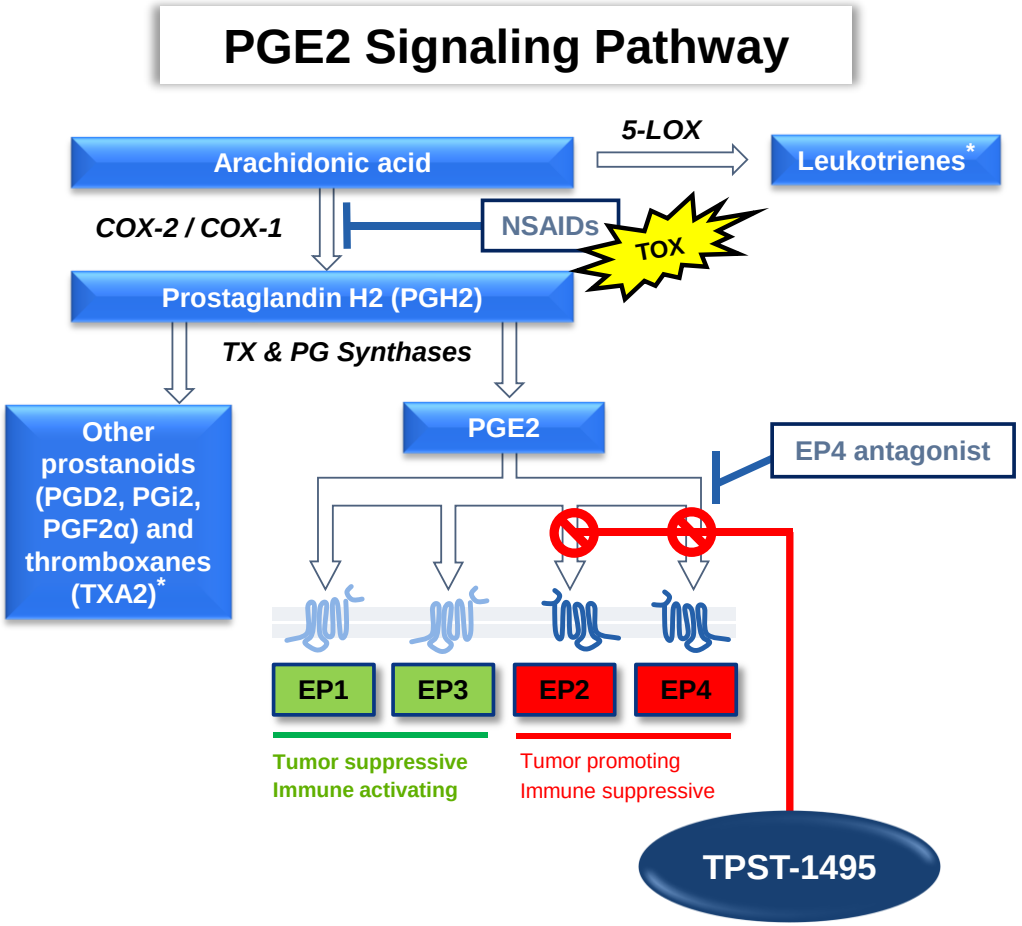
TPST-1495

First-in-Class Dual EP2/4 Antagonist

TPST-1495 is a First-in-Class[1] Dual EP2/EP4 PGE2 Receptor Antagonist

Rationally designed, based on an understanding of PGE2 signaling in cancer progression

- Prostaglandin E_2 (PGE2) has both tumor *promoting* and tumor *suppressing* activity through its 4 receptors (EP 1-4)
  - NSAIDs prevent signaling through beneficial EP receptors and have toxicity
- TPST-1495 features
  - First in class, highly specific antagonist inhibits *only* the tumor promoting EP2 and EP4 receptors
  - Oral therapy
  - Nanomolar potency[2]
  - Targets *both* tumor cells and immune suppressive cells

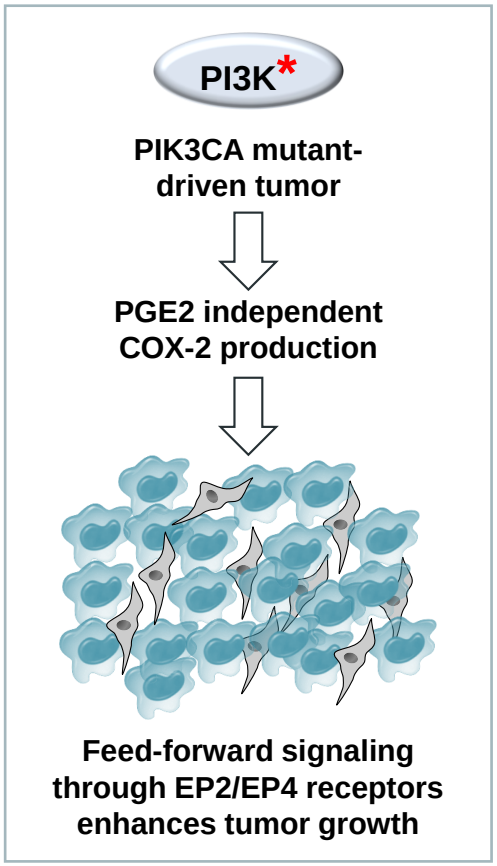


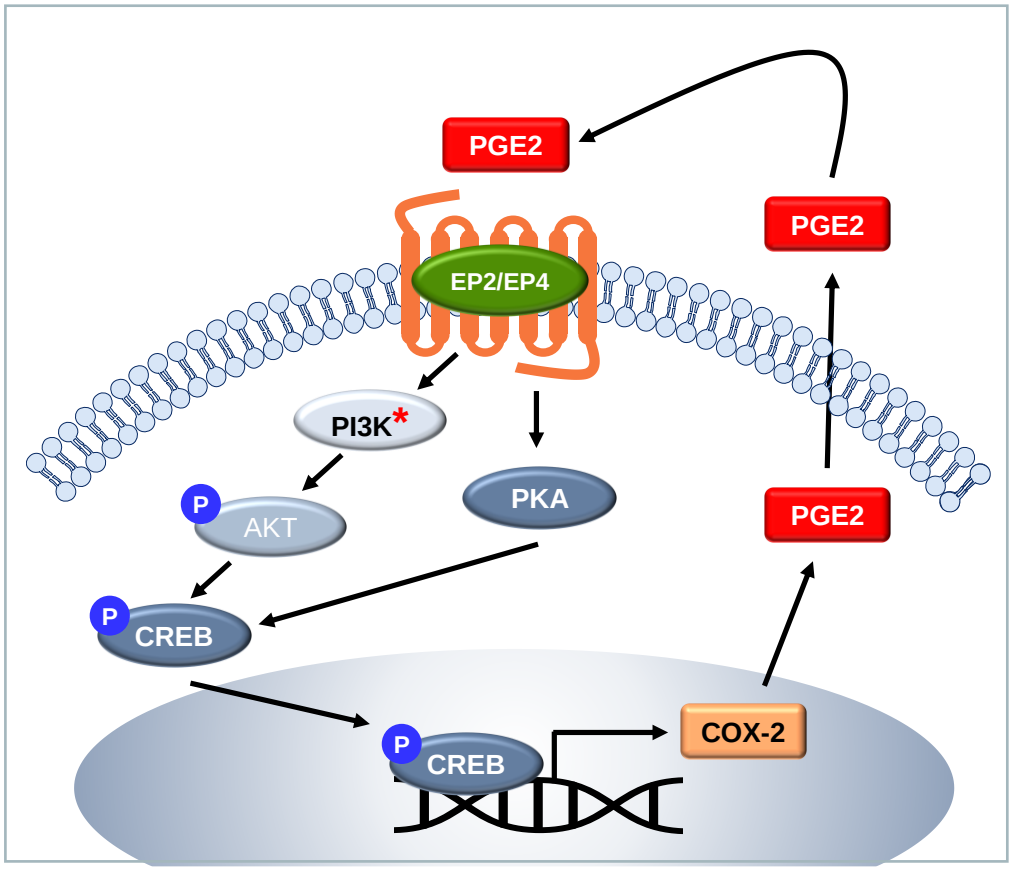
*Alterations in thromboxanes, prostacyclins and leukotrienes are associated with cardiovascular toxicity of NSAIDs

[1] If approved by FDA
[2] IC50s: 17 nM for EP2, 3 nM for EP4, and 51 nM in human whole blood assay

PIK3CA Mutation Promotes Tumor Growth & PGE2 Production

Driver mutation predictive of NSAID benefit in CRC and SCCHN

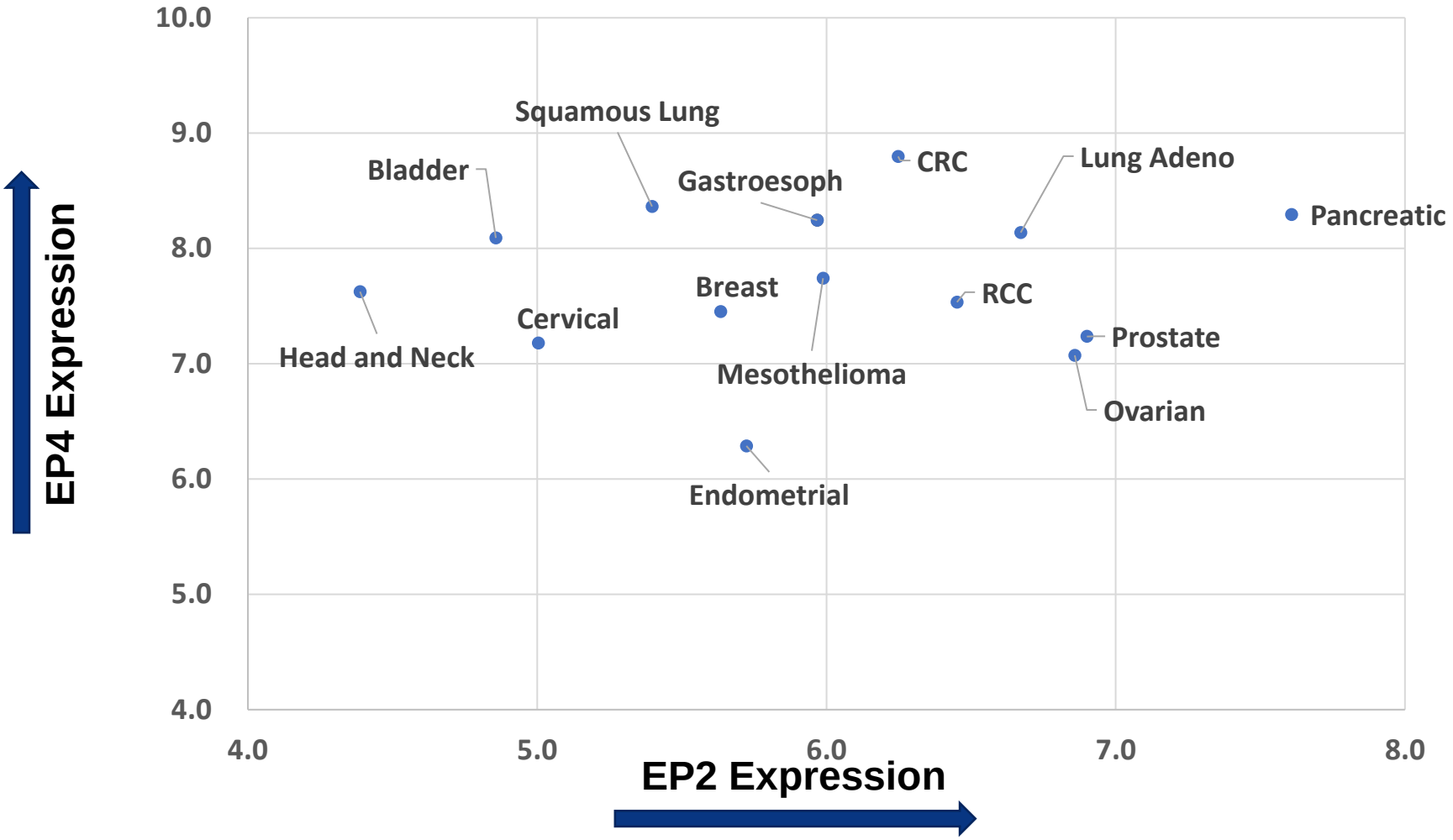




- PIK3CA tumor driver mutation constitutively activates cell proliferation and production of PGE2 and may be a biomarker for TPST-1495 responsive tumors

EP2 & EP4 Are Overexpressed in Multiple High-Need Cancers

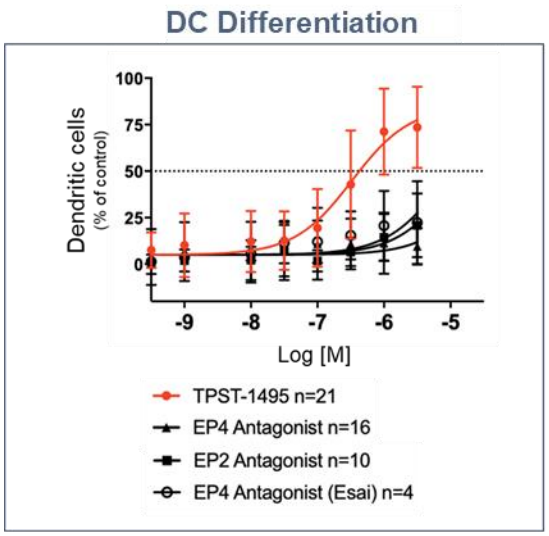
Inhibition of EP4 alone is insufficient to block PGE2 signaling for cancer therapy

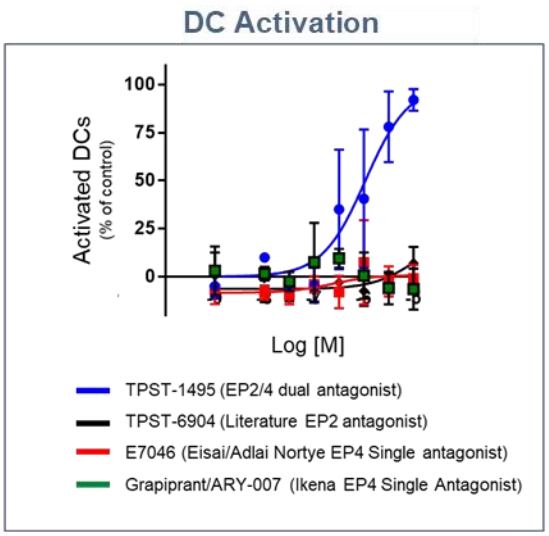


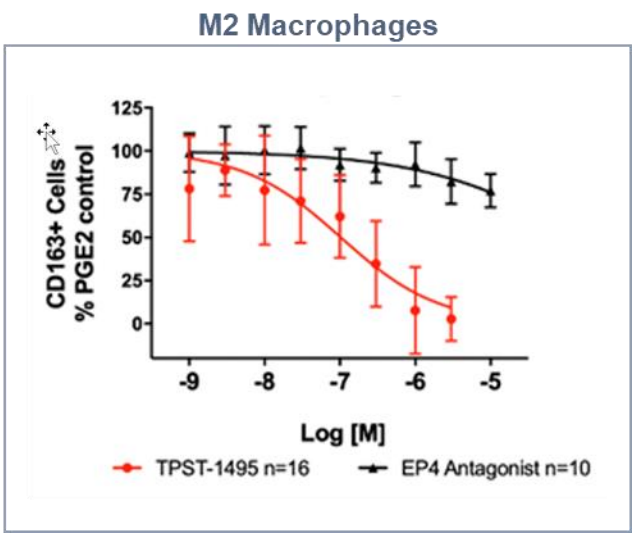
*Ratio of malignant vs normal tissue expression – medians from TCGA database

TPST-1495 is Significantly More Potent than Single EP4 or EP2 Antagonists in vitro

Head-to head comparison of DC differentiation and activation in human monocytes cultured with PGE2 and treated with TPST-1495 or single EP4 or EP2 antagonists





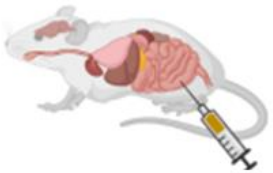


Human monocytes cultured with GMCSF + IL4 + PGE2 + EP receptor antagonist

TPST-1495 Anti-Tumor Activity is both Direct and Immune-Mediated

Dual MOA targets both tumor and immune cells

A.



LS-174T injected into cecum of NSG mice (8 wks)

TPST-1495

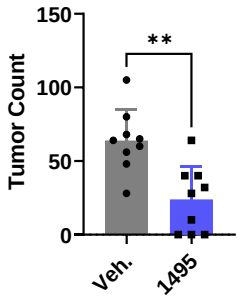
9 wks — 50 mg/kg BID

11 wks — 25 mg/kg BID

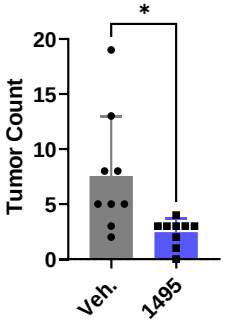
18 wks — Readout

Tumor Burden Lung & Liver

Lung Mets

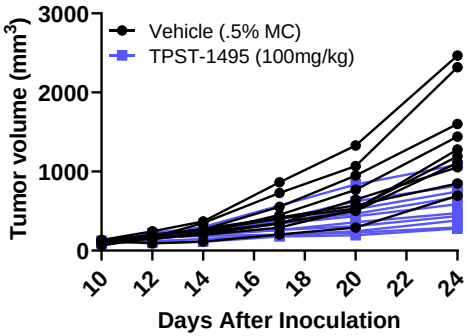


Liver Mets



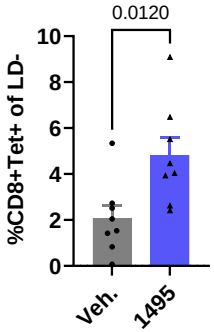
B.

Anti-tumor Efficacy

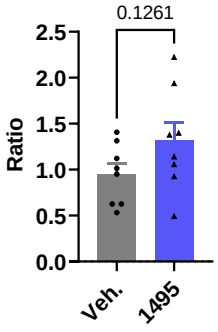


Induced Tumor-specific CD8+ T Cell Response

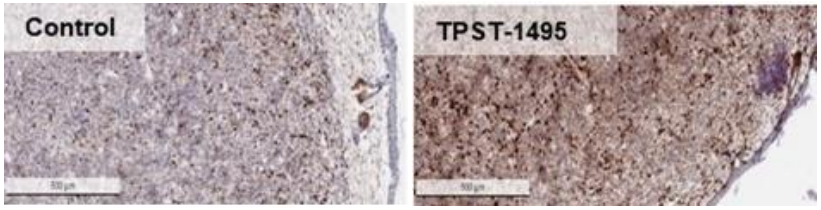
AH1+ T Cells



Teff/Treg Ratio



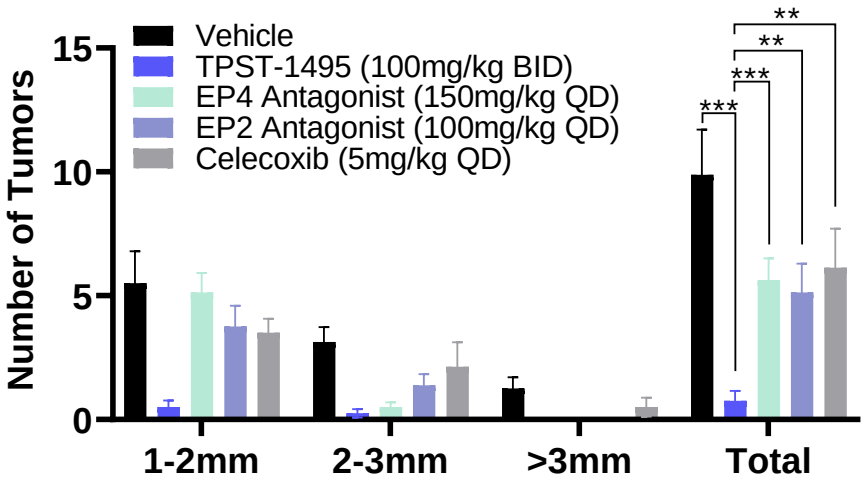
CD8+ T cell TME Infiltration



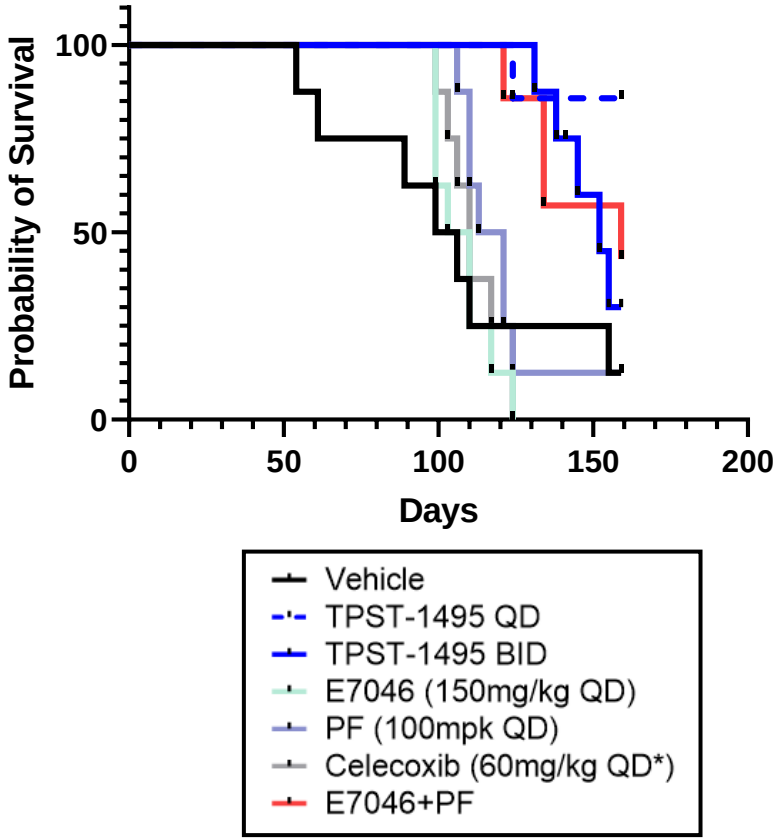
TPST-1495 Therapy Confers a Significant Survival Advantage Compared to Other Prostaglandin Pathway Inhibitors

TPST-1495 therapeutic efficacy comparison in $Apc^{Min/+}$ mouse model of CRC

Tumor burden after 3 weeks of therapy*



Survival



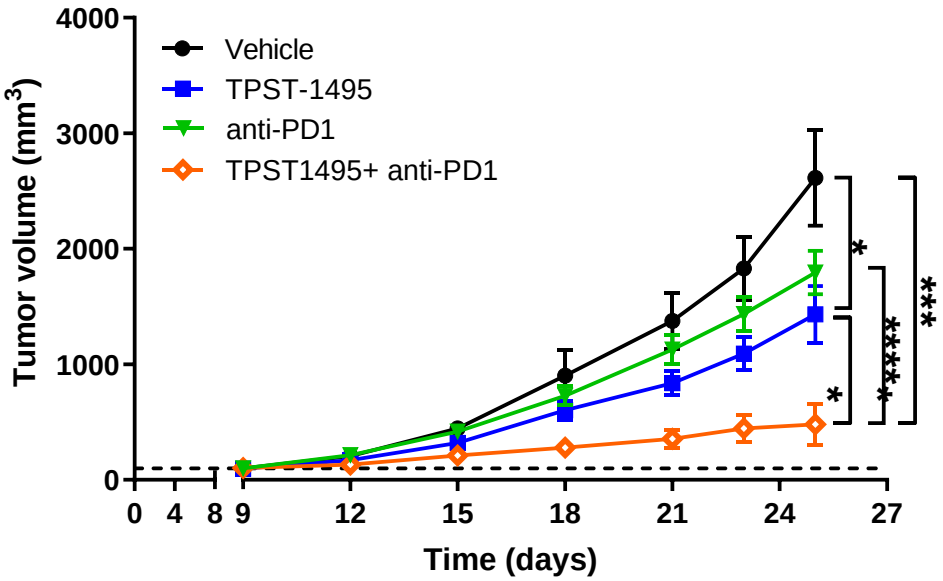
*Treatment initiated in 13 week old mice.

Compelling Rationale for Combining TPST-1495 and ICIs

Combination with checkpoint inhibitors designed to overcome “adaptive immune resistance”

- TPST-1495 therapy induces tumor-specific CD8$^+$ IFN-γ$^+$ T cells
- CD8$^+$ IFN-γ$^+$ T cells traffic to the TME and induce ***both*** PD-L1 and COX-2 on tumor cells*
- “Adaptive Immune Resistance” describes the phenomenon when tumors become resistant to ICI
- Combination of TPST-1495 and anti-PD-1 therapies may block orthogonal mechanism of tumor progression

Synergistic efficacy with TPST-1495 and anti-PD-1 combination

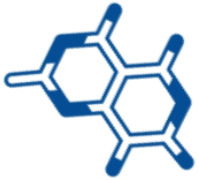


*S. Topalian lab SITC 2021 poster: “The COX-2 Pathway as a Mediator of Resistance to Anti-PD-1 Therapy”

TPST-1495 Near-Term Development Strategy

Maximize PTS for signal detection and potentially-broader development opportunity

TPST-1495



Combination with Pembrolizumab

Enrolling

- Multiple dose levels
- QD administration
- Continuous vs Intermittent dosing

RP2D

- Near-term expansion planned in targeted patient population: MSS CRC, endometrial, SCCHN and/or PIK3CA basket studies[1]
- First study planned for 2H'22[1,2]

Dose & Schedule Optimization

RP2D Expansion in Targeted Patient Populations

Monotherapy

Enrolling

- Multiple dose levels
- BID vs QD administration
- Continuous vs Intermittent dosing

RP2D

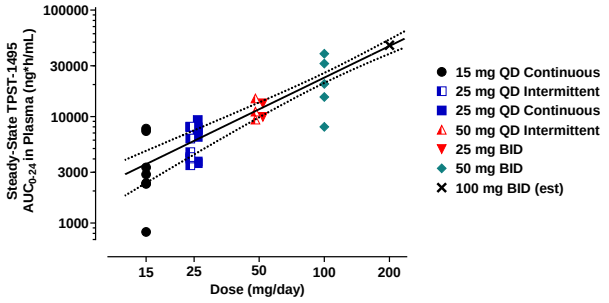
- Opportunity for program expansion in targeted patient populations: endometrial, SCCHN and/or PIK3CA basket studies[3]

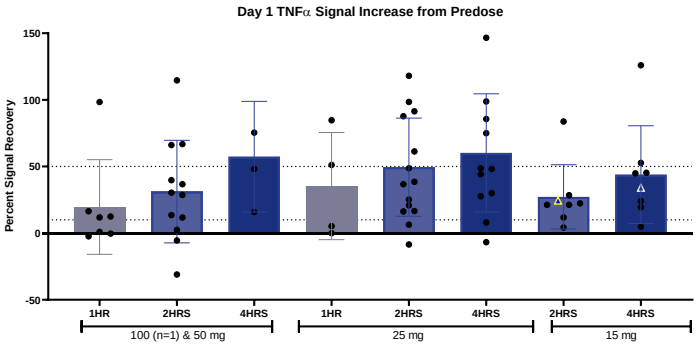
TEMPEST THERAPEUTICS

[1] Study could be either a single indication or a biomarker-based basket. [2] Timing is an estimate based on current projections. [3] With additional funding, monotherapy expansion(s) would be in select indications based on target expression and/or a PIK3CA biomarker-positive basket cohort. For either basket arm: (1) patients must have documented pathogenic mutation in PIK3CA; and (2) histologies of interest include CRC, breast, NSCLC, urothelial, gastroesophageal, anal SCC, cervical SCC

TPST-1495 Advancing Through the Clinic

- PK and PD
  - Dose-proportional exposure hits targeted levels in patients
  - Whole blood with LPS stimulation in TNFα production assay shows that TPST-1495 overcomes PGE2 suppression at all dose levels tested
- Preliminary evidence of anti-tumor activity
  - Tumor shrinkage and tumor marker reductions
- Tolerable safety profile in patients
  - QD schedule selected for optimal safety profile; no Grade 4/5 AEs and low (30%) Grade 3
  - Most common TRAEs are GI (diarrhea, abdominal discomfort, dyspepsia) – “on target” for the prostaglandin pathway
  - No cardiac or renal toxicity signal to date, consistent with differentiated mechanism of TPST-1495

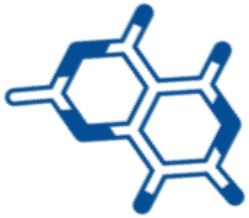




TPST-1495 Summary & Next Steps

First in class, oral, potent, specific antagonist of PGE2 EP2/EP4 receptors

TPST-1495



Early Phase 1 data show:

- Robust exposure
- On-target PD activity
- Tolerable safety profile
- Preliminary evidence of anticancer activity

- Opportunity for broad expansion at RP2D in targeted patient populations, including PIK3CA mutation-based basket study
- Combination with pembrolizumab planned as first targeted-patient expansion study in H2'22[1]

[1] Timing is an estimate based on current projections

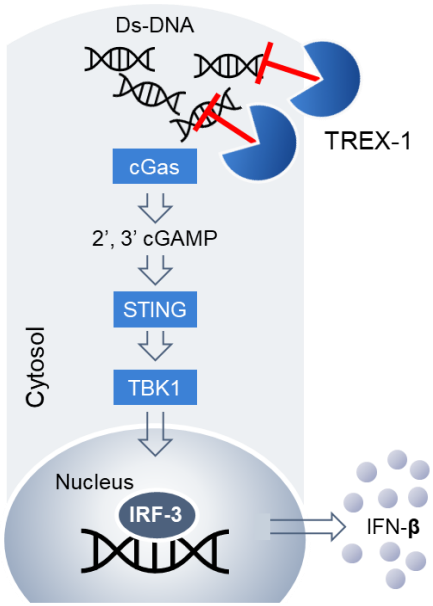
TREX-1

Optimal Approach to Target STING

TREX1 Inhibition: The Optimal Approach to Target STING

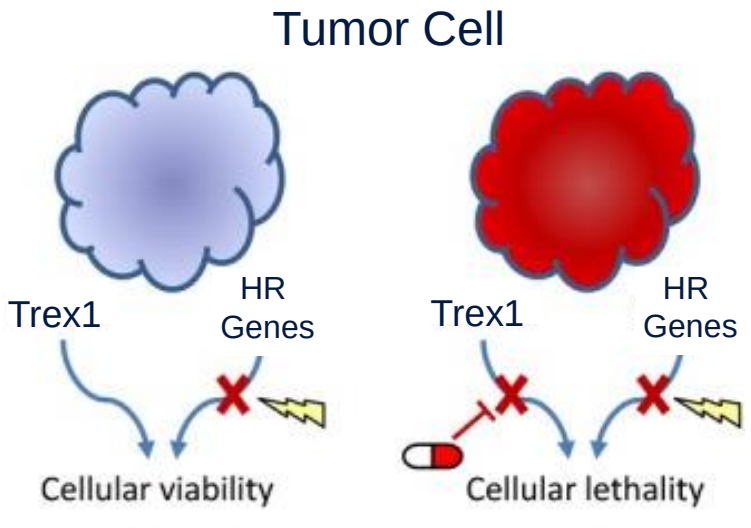
Two distinct MOA: TREX1 not only prevents STING activation, but also DNA repair

Immune Activation Via STING Pathway



TREX1 inhibition activates innate immunity by increasing dsDNA concentrations that can be sensed by STING pathway

Tumor Cell Viability



Homologous recombination (HR) deficient tumors may be susceptible to TREX inhibition due to TREX1's role in DNA repair

Adopted from Thompson et. Al. Pig Cell Mel Res, 2017

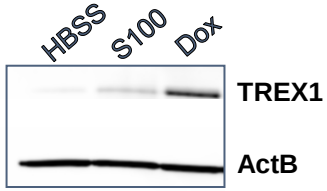
In Vivo Activity with TREX1 Inhibitor Lead Series Compound

TREX1 inhibitor-dependent reduction of tumor volume

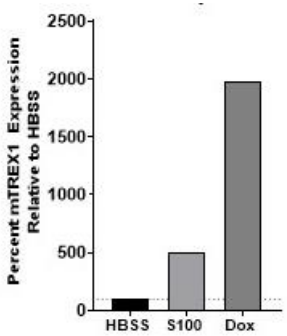
Experimental Rationale:

Doxorubicin (Dox) induces DNA strand breaks in tumor cells and induces TREX1 expression. Inhibition of TREX1 with TPST-994 leads to activation of the cGAS/STING pathway and anti-tumor efficacy

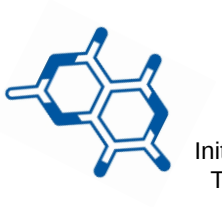
Doxorubicin induces TREX1 in CT26 tumors

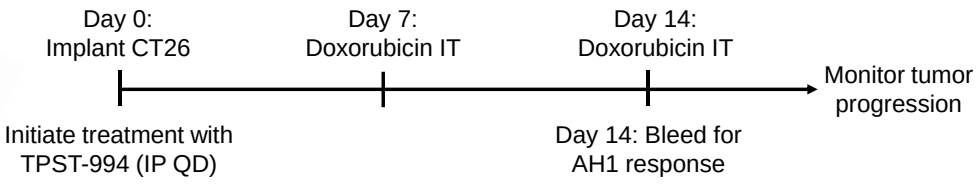


TREX1 Relative Protein Expression

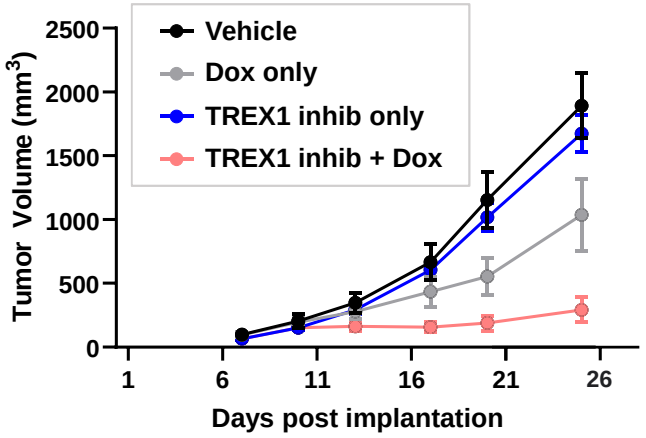


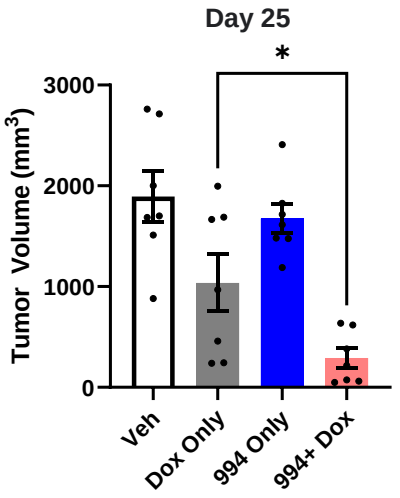
*S100 is a direct STING agonist





CT26 tumor volume

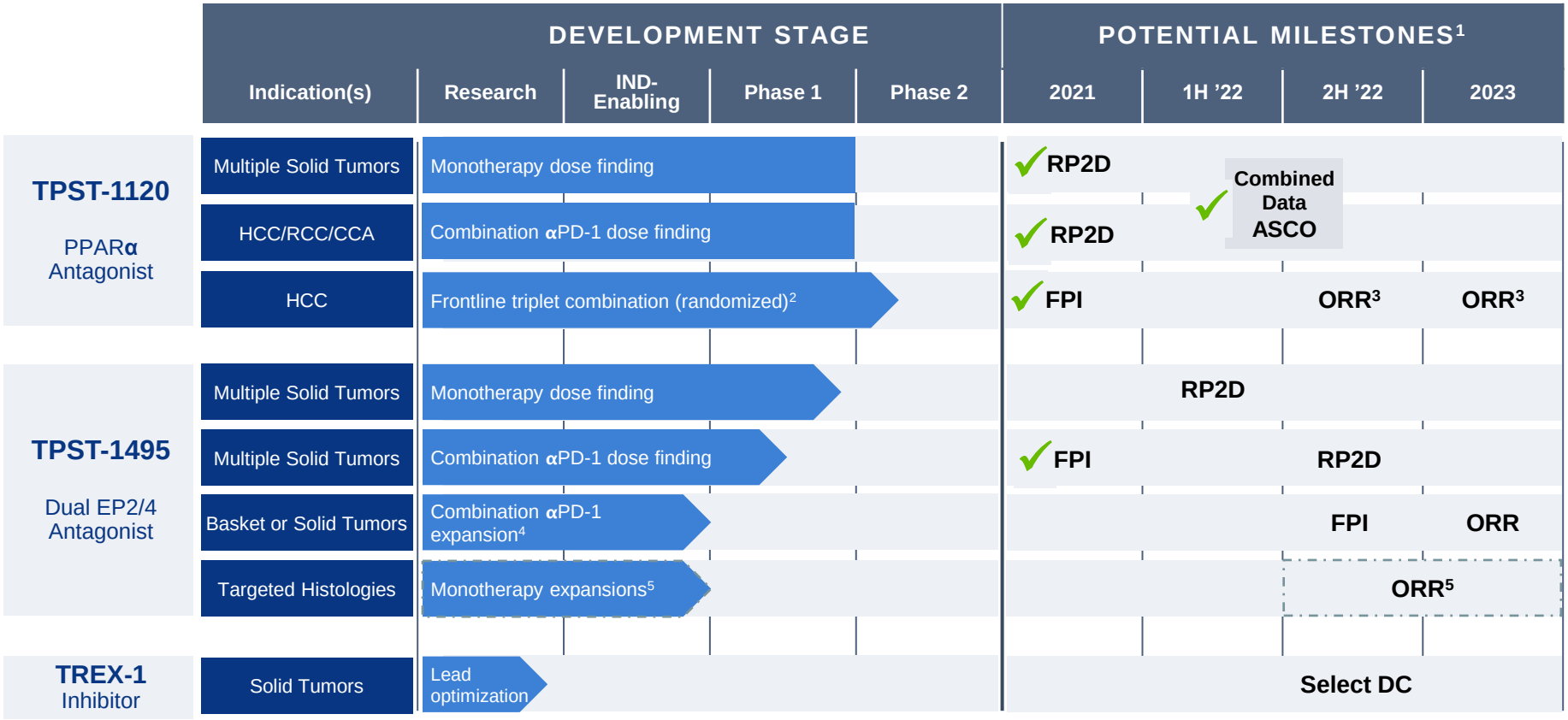




Newsflow

Multiple Potential Catalysts Through 2022-2023

Diversified clinical and pre-clinical portfolio engenders a broad opportunity



"RCC" renal cancer; "HCC" hepatocellular carcinoma; "CCA" cholangiocarcinoma "FPI" first patient in; "RP2D" recommended Ph2 dose

[1] Timing is an estimate based on current projections. [2] Pursuant to a collaboration with Roche; TPST retains all product rights [3] Based on partner projections, ORR on 40 pts in triplet arm expected by YE/early 2023, with additional data in 2023 (including on additional patients, if study expanded) [4] Expansion study could be either a single indication or biomarker-based basket [5] With additional funding, monotherapy expansion would be in select indications based on target expression and/or a biomarker-positive basket cohort; ORR data expected from monotherapy expansion arms within 12-18 months of study commencement, depending on the histology

Leadership Team Experienced in Drug Development

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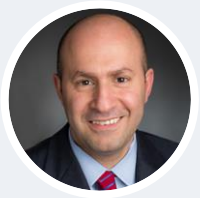
Harvard Medical School



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