



TEMPEST
THERAPEUTICS

Company Overview

April 2024

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. All statements that are not historical facts are forward-looking statements, including any statements regarding the design, initiation, progress, timing, scope and results of clinical trials, the ability of Tempest Therapeutics to advance discussions with potential partners to explore the development of TPST-1120, the anticipated therapeutic benefit, opportunity to improve patient care, and regulatory development of Tempest Therapeutic’s product candidates, Tempest Therapeutic’s ability to deliver on potential value-creating milestones, the potential use of Tempest Therapeutic’s product candidates to treat additional indications, Tempest Therapeutic’s ability to achieve its operational plans, and the sufficiency of Tempest Therapeutic’s cash and cash equivalents. 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-K filed by Tempest Therapeutics with the Securities and Exchange Commission on March 19, 2024. 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.



TPST-1120 Data Support Pivotal Study in First-Line Liver Cancer Emerging as a Potential Franchise

Programs

***Randomized 1L HCC data are superior
to standard of care***

- ✓ ORR of 1120 arm is independent of PD-L1 or inflamed tumor status
- ✓ OS HR favors 1120 and median not reached
- ✓ Biomarker data further support dual MOA of TPST-1120
- ✓ Beyond HCC: positive data in RCC & CCA
- ✓ Three additional programs - diversified portfolio

Strategy

Focused on indications
with potential for
substantial impact

Programs fully owned;
BD optionality

Team

Experienced in novel
drug discovery,
development, and
delivering value

Catalysts

Multiple potential value-
creating milestones
through 2024

First First-in-Class Oncology Pipeline with Broad Potential

Spanning early-stage novel targets to late-stage, pivotal development

| | | Indication(s) | STAGE OF DEVELOPMENT | | | | | Status |
|--|---|--|----------------------|--------------|------------------------------|---------|------------------------|--------|
| | | | Research | IND-Enabling | Phase 1 | Phase 2 | Phase 3 | |
| Clinical Programs | | | | | | | | |
| TPST-1120 PPAR α Antagonist | Multiple Solid Tumors | Monotherapy dose & schedule finding | | | ASCO Oral Presentation | | Completed | ✓ |
| | HCC/RCC/CCA | Combination α PD-1 dose and schedule finding | | | | | Completed | ✓ |
| | HCC | First-line triplet combination (randomized) ¹ | | | | | Full Data | ✓ |
| TPST-1495 Dual EP2/4 Antagonist | Multiple Solid Tumors | Monotherapy & Combination α PD-1 | | | ASCO Presentation | | Completed | ✓ |
| | Endometrial | Combination α PD-1 | | | | | Ongoing | |
| | FAP | Monotherapy | | | | | FPI 2H'24 ² | |
| Discovery & Research Programs | | | | | | | | |
| Novel Targets | Solid Tumors & Hematologic Malignancies | | | | | | Ongoing | |



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

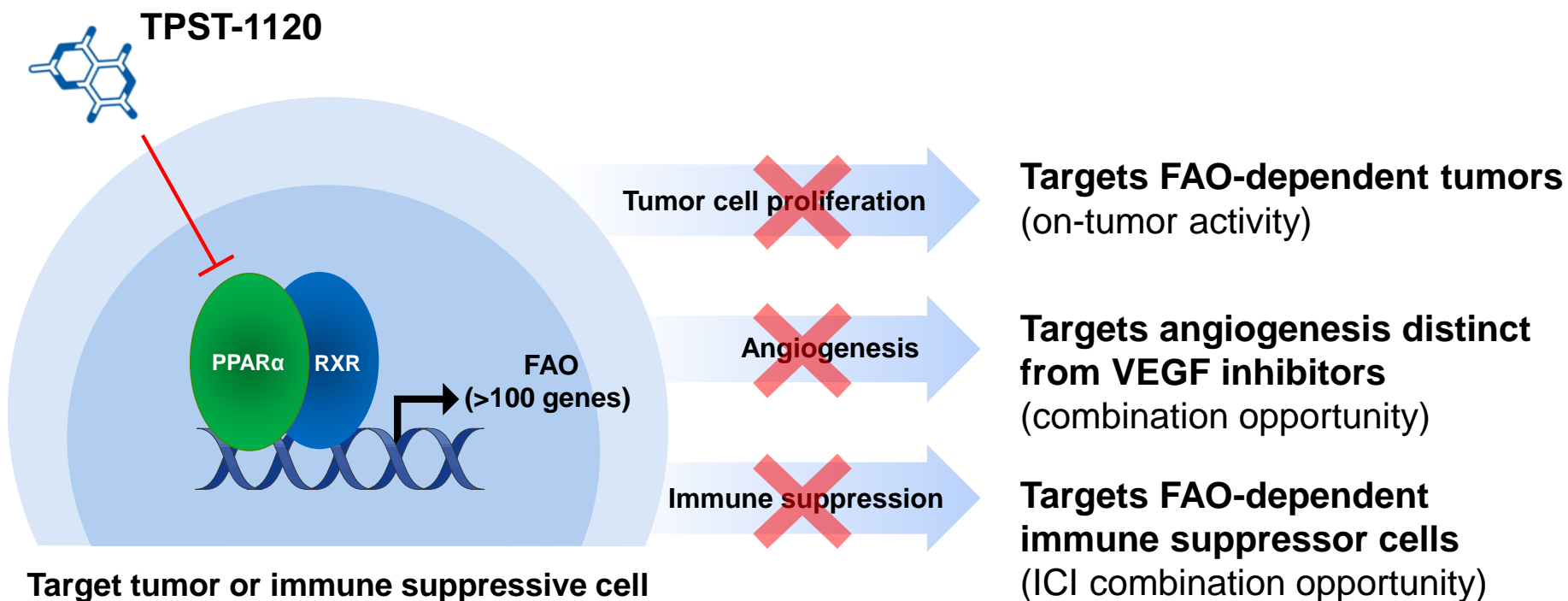
First in class if approved by FDA. ¹ Pursuant to a collaboration with Roche; TPST retains all product rights. ² Initial approval by NCI received; awaiting final approval.

TPST-1120

First-in-Class PPAR α Antagonist

TPST-1120: First-in-Class¹ PPAR α Antagonist

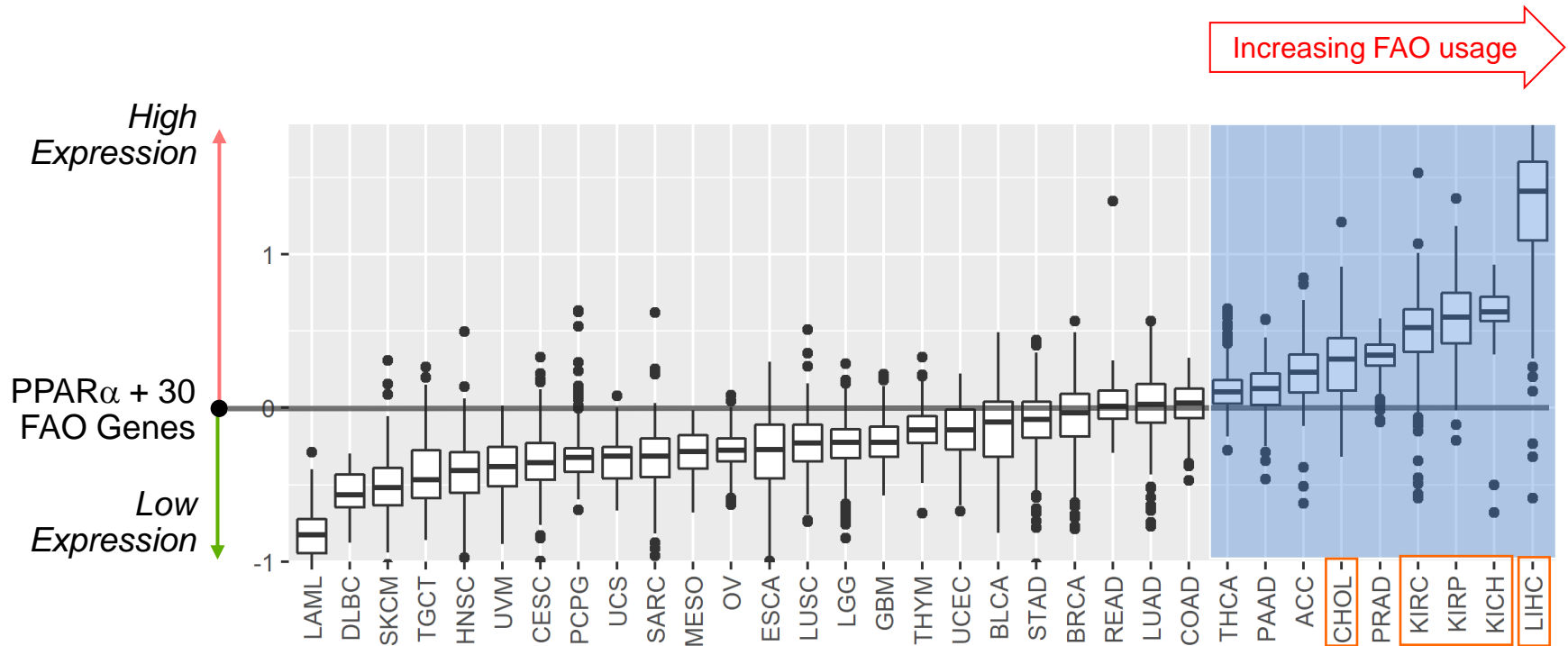
Targets both tumor cells and immune suppressive cells



PPAR α : Peroxisome Proliferator-Activated Receptor alpha

FAO-Dependent Tumors Inform Clinical Strategy

TCGA-based analysis of tumor metabolic gene expression profiles



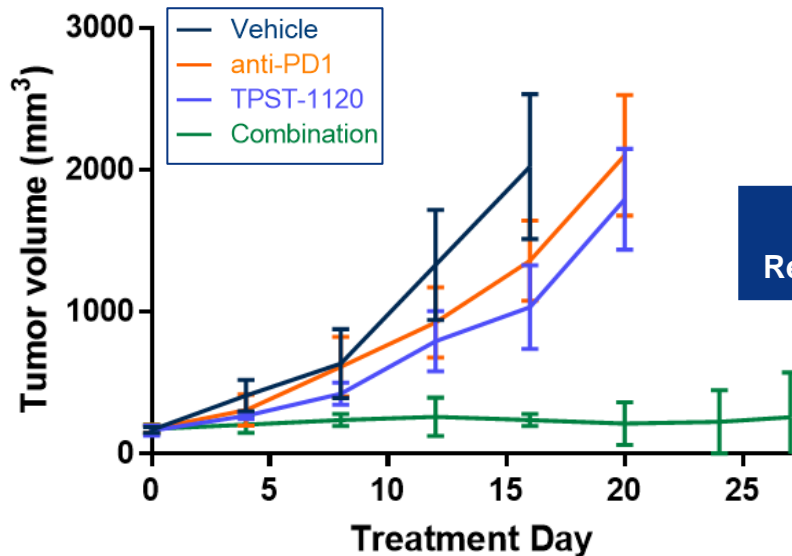
Focus on FAO-dependent tumors: **HCC, RCC**, prostate, **cholangiocarcinoma**, pancreas, NSCLC, CRC

Positive data in HCC, RCC & CCA

Durable Responses in Combination with α -PD-1

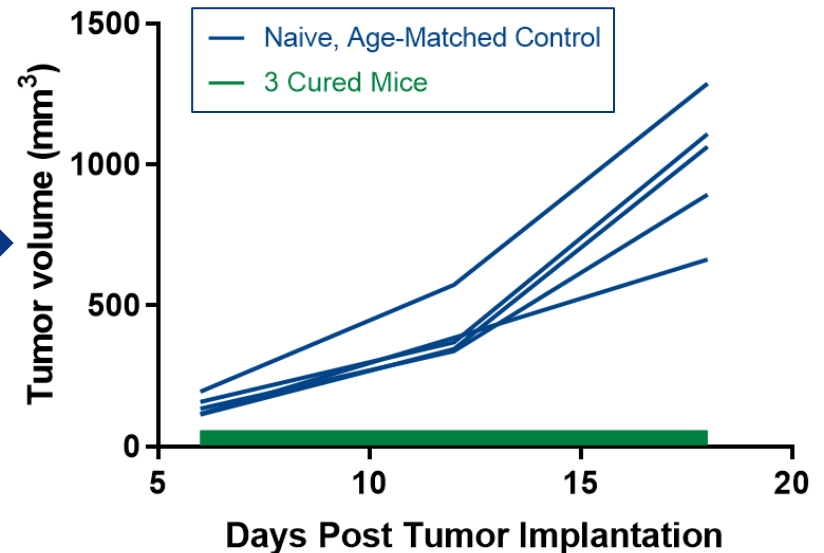
MC38 colorectal cancer tumor model, C57BL/6 immunocompetent mice

TPST-1120 + anti-PD1 treatment



Tumor Re-challenge

Tumor re-challenge

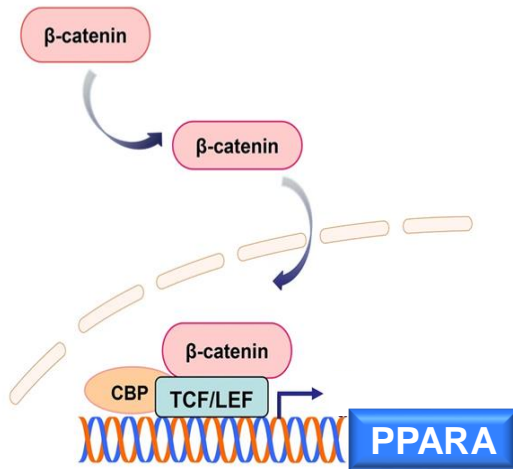


C57BL/6 mice bearing 150 mm³ MC38 flank tumors treated with TPST-1120 30 mg/kg BID and 200 μ g α -PD-1 Q3D

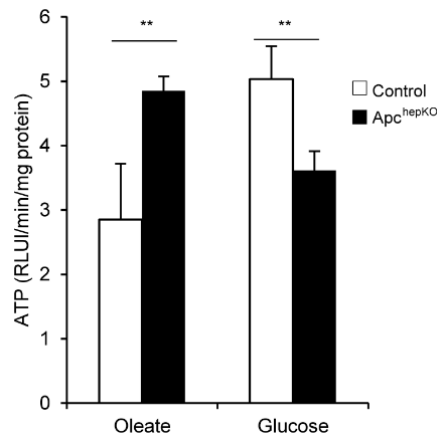
Activated β -Catenin Pathway Induces PPAR α Expression and Reliance on FAO

Identifying cancers with increased sensitivity to TPST-1120

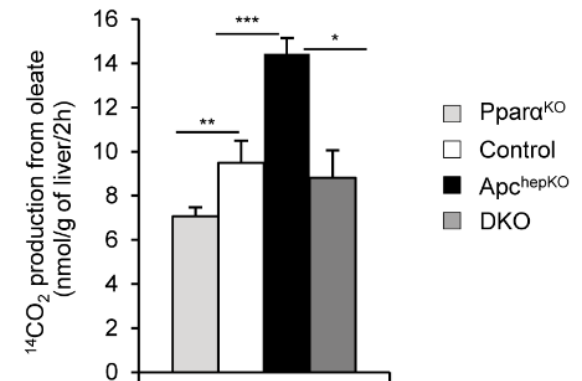
Activated β -catenin pathway



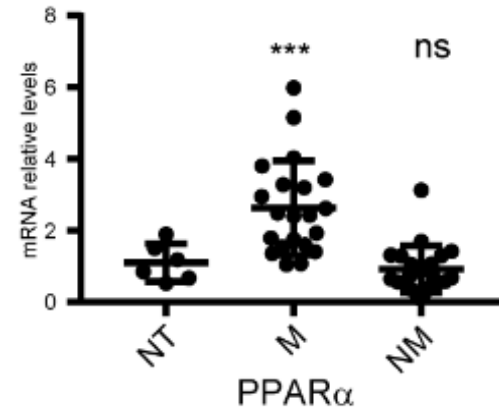
Increased FAO in β -catenin-activated mouse hepatocytes



Increased FAO in β -catenin-activated mouse liver is PPAR α -dependent



Enhanced PPAR α expression in mutated *CTNNB1* HCC



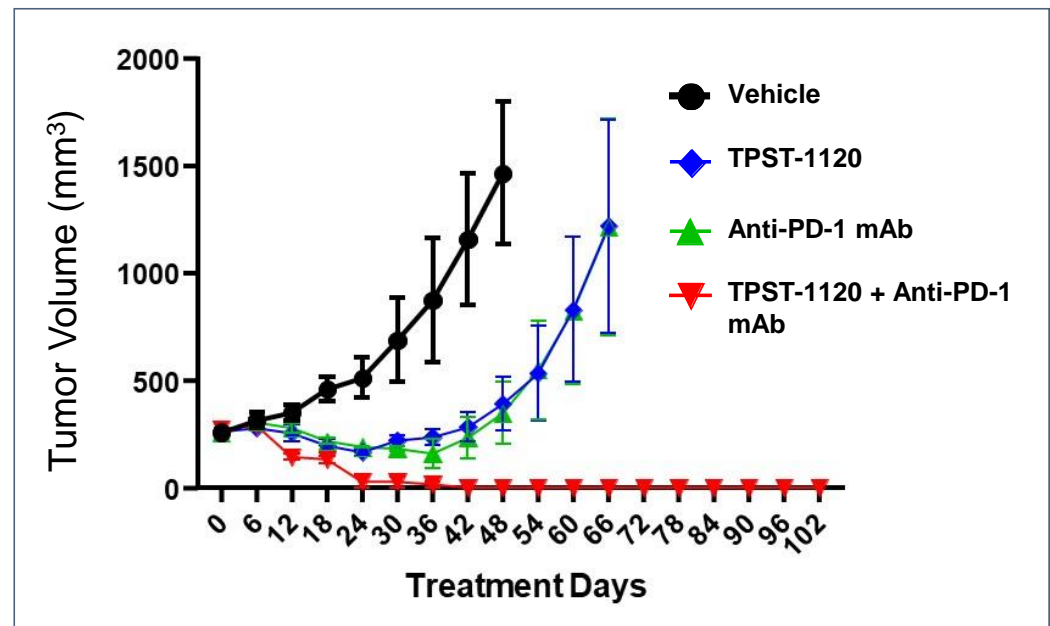
NT: Normal liver tissue
M: Mt *CTNNB1* HCC
NM: Non-mt *CTNNB1* HCC

Preclinical HCC Data Support Clinical Development Strategy

β -catenin pathway frequently activated in HCC: Potential Biomarker

- Wnt/ β -catenin pathway is critical for stem cell regeneration, and tumorigenesis (i.e., EMT)
- Activation of WNT/ β -catenin pathway occurs frequently in HCC: 40-70%^{1,2,3}
- PPAR α expression is higher in CTNNB1-mutated human HCC
- β -catenin activated HCC confers dependence on FAO for metabolism
- Available genetic tests for CTNNB1, APC and modulators of β -catenin pathway

Efficacy in syngeneic β -Catenin-driven hepatocellular carcinoma model*

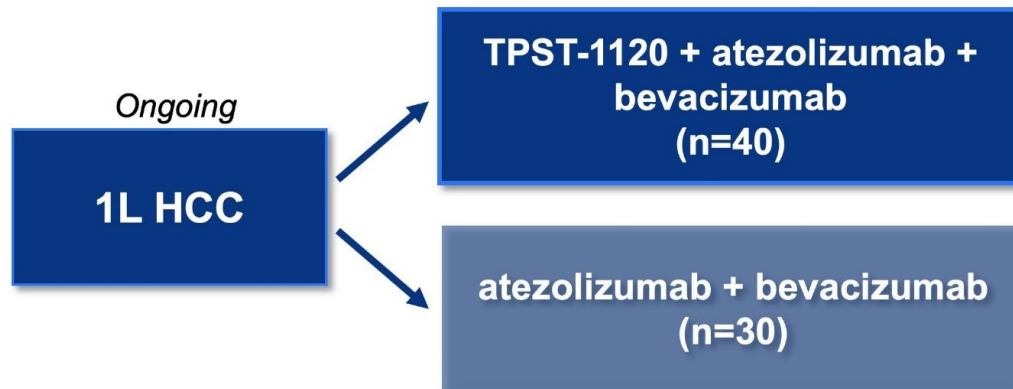


TPST-1120 Randomized Clinical Data

First-Line HCC Compared to Standard of Care

TPST-1120 in Front-Line Phase 1b/2 HCC Randomized Study

Global study* accelerated program to pivotal readiness; Tempest retains all rights to program



- Standard of care 1L regimen +/- TPST-1120
- Ongoing multi-arm global randomized study¹
 - US, Asia, Europe
 - 26 sites
 - 7 countries
- Primary Efficacy Endpoint
 - Confirmed ORR (RECIST 1.1)
- Secondary Efficacy Endpoints
 - include PFS and OS
- Comprehensive Safety Endpoints

TPST-1120 Arm Improves All Efficacy Endpoints vs. Control

| | atezo/bev N=30 | TPST-1120 + atezo/bev N=40 |
|----------------------------------|-------------------------|-------------------------------|
| Confirmed ORR (ITT population) | 13.3% | 30% |
| PFS HR 0.7 | Median 4.27m (2.8, 7.3) | 7m (5.6, 13.8) |
| OS HR 0.59 | Median 15.1m | NR |
| PD-L1 negative Confirmed ORR | 7% | 27% |
| β-catenin mutation Confirmed ORR | N/A ¹ | 43% (100% DCR) |

- **Biomarkers and pharmacodynamic data support MOA of TPST-1120**

- Consistent with mechanism, β-catenin activation and FAO upregulation preferentially improve activity in TPST-1120 arm vs atezo+bev control
- Consistent with mechanism, TPST-1120 improves activity of atezo+bev in PD-L1 negative and immune desert/excluded phenotype

- **Favorable safety profile**

- No increase in high grade AEs, treatment discontinuation, or dose holds/reductions on TPST-1120 arm vs atezo + bev arm; no decrease in atezo or bev dose intensity on TPST-1120 arm

- **Pivotal study of TPST-1120 in 1L HCC is the next appropriate step²**

Subject Disposition Continues to Favor TPST-1120 Arm

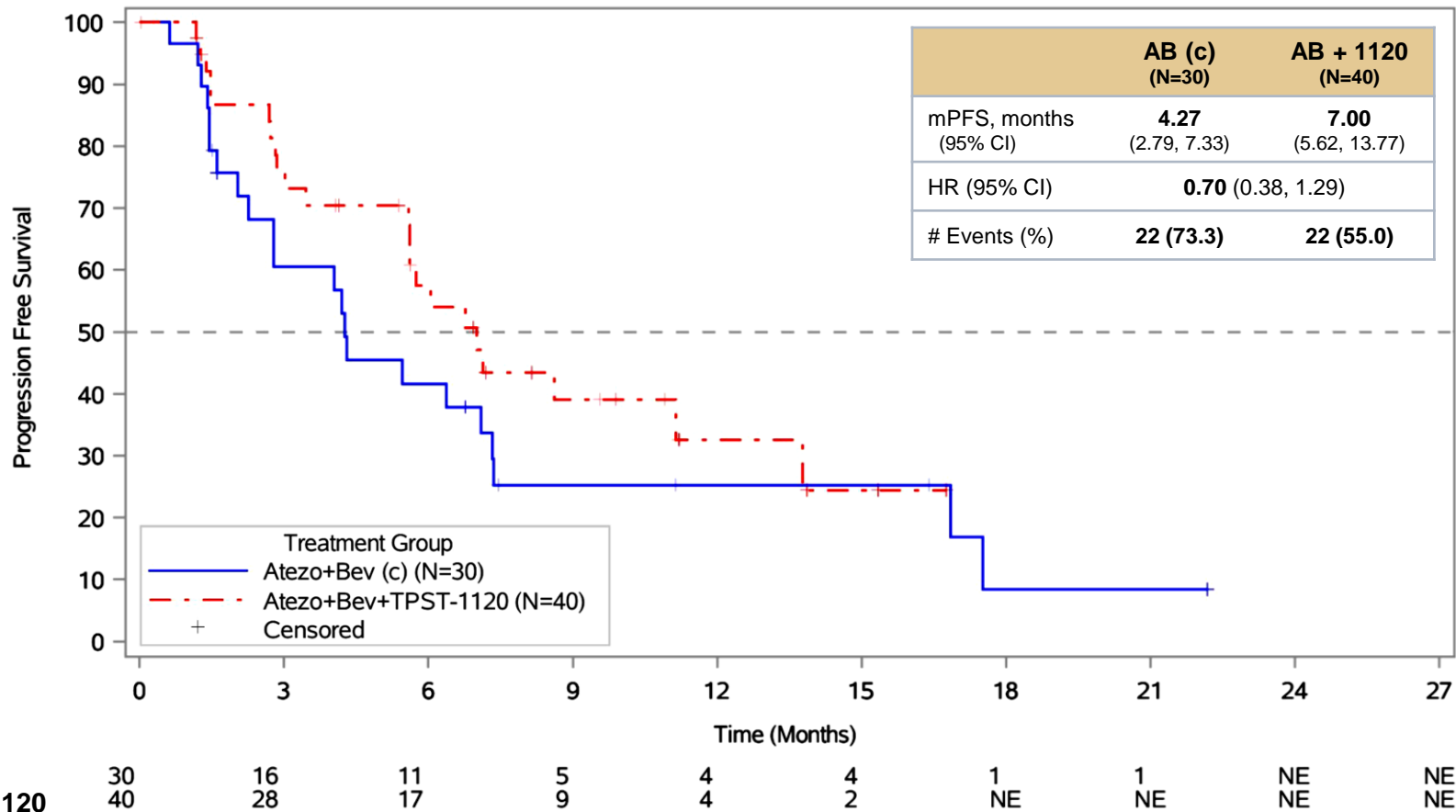
Patients are on drug and surviving longer with the addition of TPST-1120

| | Atezo+Bev (c) (N=30) | % | TPST-1120+ Atezo+Bev (N=40) | % |
|-------------------------------------|-------------------------|-------|-----------------------------------|-------|
| On Study | 14 | 46.7% | 29 | 72.5% |
| On Treatment | 5 | 16.7% | 16 | 40.0% |
| Off Treatment in survival follow-up | 9 | 30.0% | 13 | 32.5% |
| Off Study | 16 | 53.3% | 11 | 27.5% |
| Death | 14 | 46.7% | 10 | 25.0% |
| Withdrew Consent | 2 | 6.7% | 1 | 2.5% |

- On Study Treatment: 40% (16) of TPST-1120 subjects vs 16.7 (5) of control subjects
- Subjects Alive: 75% (30) of TPST-1120 subjects vs 53.3% (16) of control subjects
- Median Duration of Follow-up: TPST-1120 arm **9.23 mo**, Atezo+Bev arm **9.89 mo**

PFS: Important Endpoint Favors TPST-1120 Arm

TPST-1120 + Atezo/Bev vs. Atezo-Bev

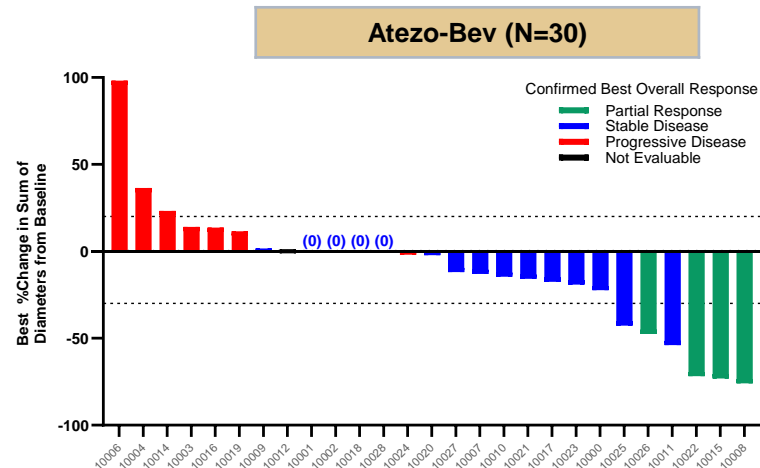
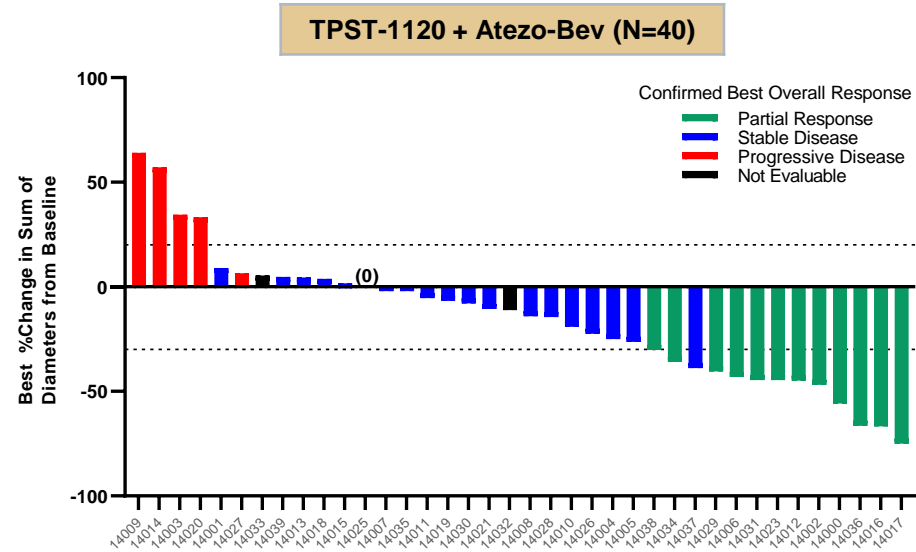


TPST-1120 More than Doubles Response Rate of Atezo+Bev

Confirmed ORR of 30% vs. 13.3%

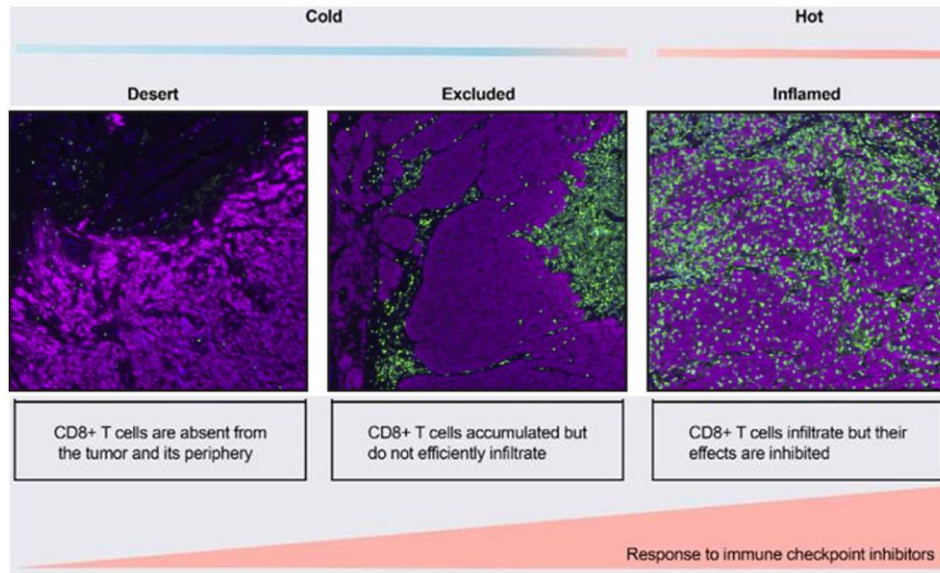
| TPST-1120 + Atezo-Bev, N=40 (% N) | |
|-----------------------------------|------------------|
| Responders | 12 (30.0) |
| Partial Response | 12 (30.0) |
| Stable Disease | 18 (45.0) |
| Progressive Disease | 6 (15.0) |
| Not Evaluable | 3 (7.5) |
| Missing | 1 (2.5) |
| Pts with tumor shrinkage | 26 (65) |

| Atezo-Bev, N=30 (% N) | |
|--------------------------|-----------------|
| Responders | 4 (13.3) |
| Partial Response | 4 (13.3) |
| Stable Disease | 15 (50.0) |
| Progressive Disease | 8 (26.7) |
| Not Evaluable | 1 (3.3) |
| Missing | 2 (6.7) |
| Pts with tumor shrinkage | 15 (50) |



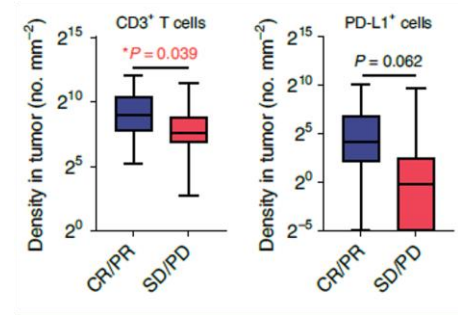
TPST-1120 Improves ORR in Two Difficult Sub-populations

CTNNB1 mutants and PD-L1 negative HCC patients both respond with TPST-1120 therapy

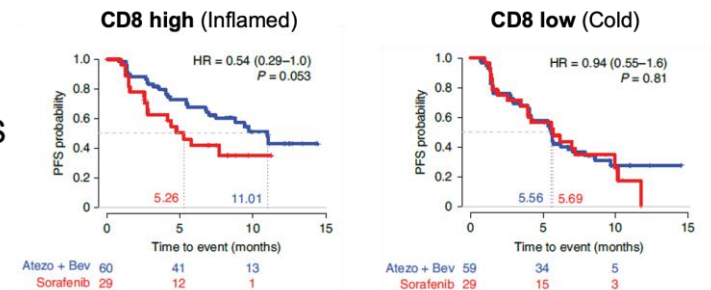


Tumor images representing 3 patterns of T cell infiltration visualized by CD3+ T cells (green) and a tumor marker (magenta). Van der Woude Trends in Cancer 2017.

ORR
Atezo/Bev



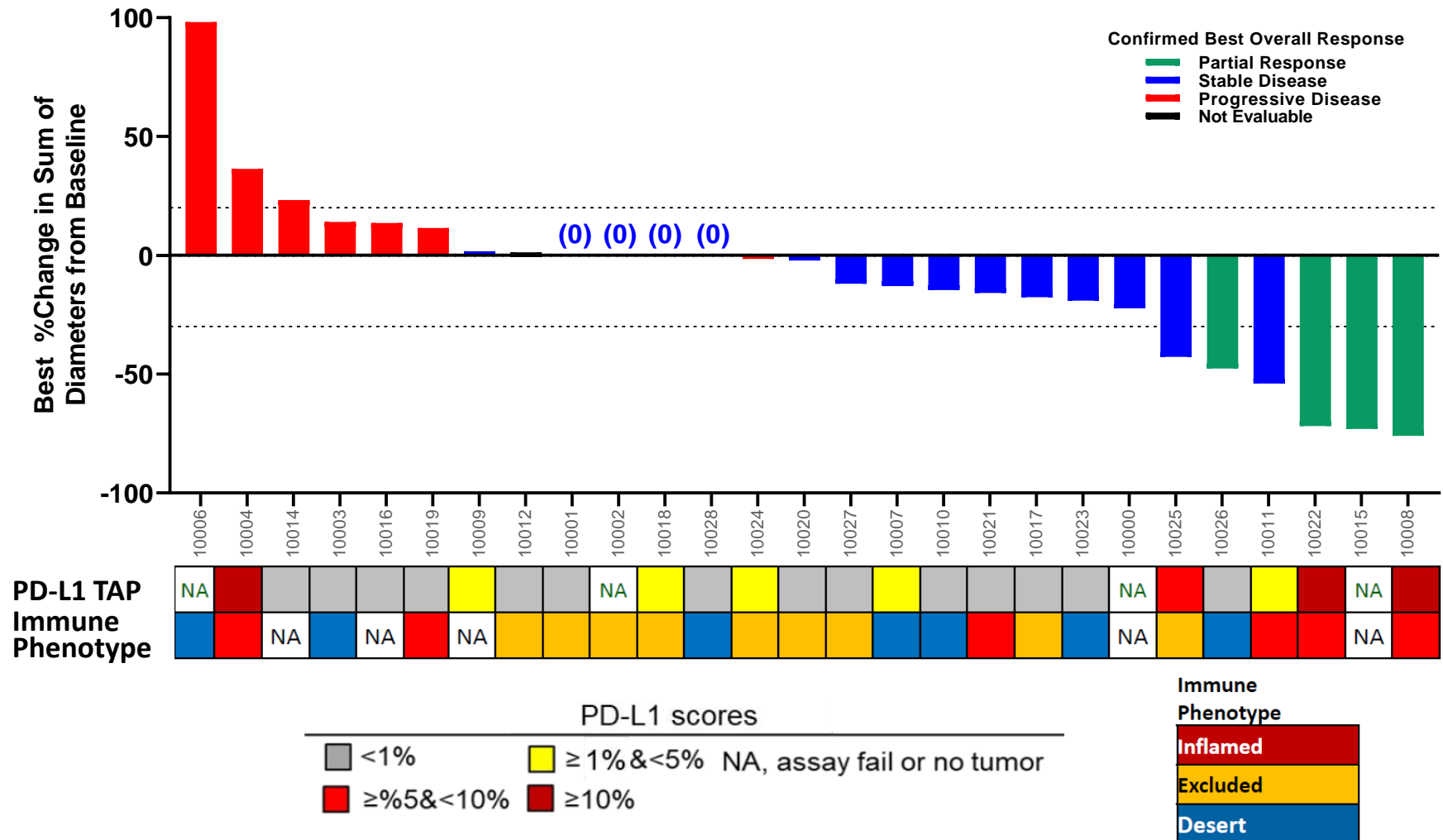
PFS



- The majority (60-70%) of HCC tumors are non-inflamed and/or PD-L1 negative ^{1,2,3}
- *CTNNB1* mutations in HCC are associated with non-inflamed tumors and ICI resistance^{4,5}
- Atezo/bev activity is reduced in HCC patients with immune cold and PD-L1 negative tumors⁶

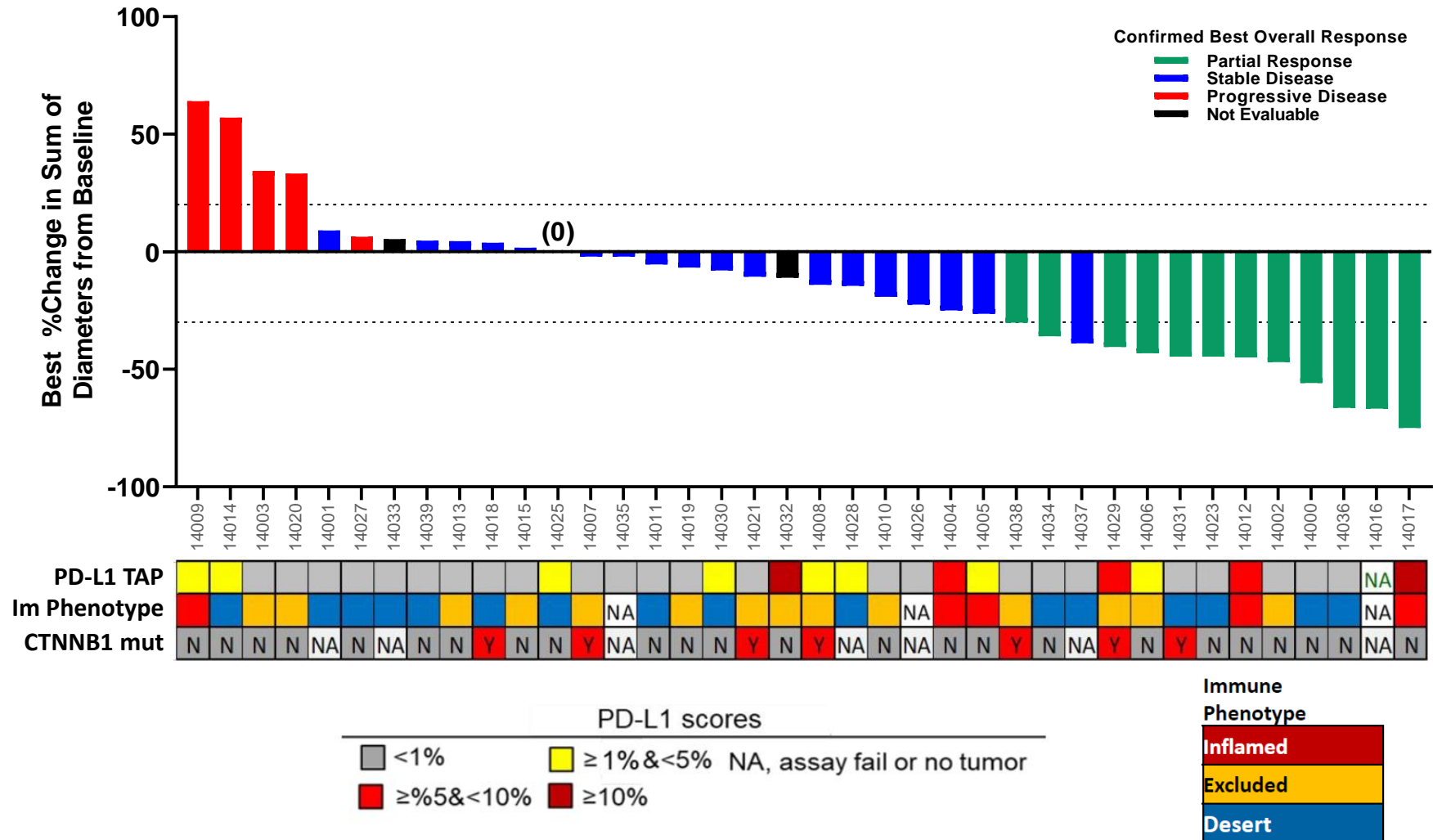
PD-L1+ and/or Inflamed Phenotype Enriched in Control Arm Responses

Atezo + Bev biomarker associations



TPST-1120 Arm Responses Independent of PD-L1+ and/or Inflamed Tumor Status

43% ORR and 100% DCR in CTNNB1-mutated disease: in-line with TPST-1120 MOA



Safety for TPST-1120 + Atezo + Bev

Triplet arm is well tolerated compared to atezo + bev doublet control arm

| | Atezo + Bev (n=30) | TPST-1120 + AB (n=40) |
|--------------------------------|------------------------------|---------------------------------|
| Fatal AEs (Grade 5) | 4 (13.3%) | 3 (7.5%) |
| Grade 3-4 AEs | 18 (60%) | 21 (52.5%) |
| AEs leading to | | |
| Treatment discontinuation | 5 (16.7%) | 3 (7.5%) |
| Dose Modification/Interruption | 8 (26.7%) | 7 (17.5%) |
| Related SAE | 8 (26.7%) | 9 (22.5%) |
| irAEs* | 20 (66.7%) | 27 (67.5%) |

*hepatitis, rash, infusion rxn, colitis, hypothyroidism, hyperthyroidism, diabetes, pneumonitis

| Drug Dose Intensity | | | |
|----------------------------|---------------------|--------------------|------------------|
| Study Arm | Atezolizumab | Bevacizumab | TPST-1120 |
| Control | 88.9% | 83.3% | NA |
| TPST-1120 | 93.2% | 84.5% | 93.6% |

Balanced Demographics and Baseline Characteristics

Generally balanced, although multiple variables favor the control arm

| Demographic | Result | Atezo+Bev (c) (N=30) | TPST-1120 + Atezo+Bev (N=40) |
|--|----------------|-------------------------|------------------------------------|
| Age group (yr) | >=65 | 12 (40.0%) | 25 (62.5%) |
| Sex | Male | 26 (86.7%) | 33 (82.5%) |
| ECOG Status | 0 ^a | 22 (73.3%) | 26 (65.0%) |
| Disease due to viral hepatitis ^b | Yes | 16 (53.3%) | 26 (65%) |
| Macrovascular Invasion and/or Extrahepatic spread | Yes | 14 (46.7%) | 21 (52.5%) |
| Baseline alpha-feto protein ≥ 400 ug/L | ≥ 400 ug/L | 17 (56.7%) | 16 (40%) |
| Region of enrollment | Asia (vs ROW) | 8 (26.7%) | 14 (35.0%) |
| Baseline neutrophil to lymphocyte (NLR) ratio ^c | ≥5 | 4 (13.3%) | 11 (27.5%) |
| PD-L1 Negative | Neg (TAP<1) | 15 (60%) ^d | 26 (67%) ^e |

ECOG status, MVI/EHS, Age, baseline NLR, PD-L1 status all favor the control arm, whereas AFP and region of enrollment favor the 1120 arm

^a ECOG status 0 indicates healthier patients

^b IMbrave150 update showed that atezo+bev regimen performed similarly in viral vs non-viral disease¹

^c A number of recent studies have reported that baseline NLR is predictive of ORR and/or OS in HCC with atezo + bev regimen²

^d25 subjects PD-L1 evaluable; ^e39 subjects PD-L1 evaluable

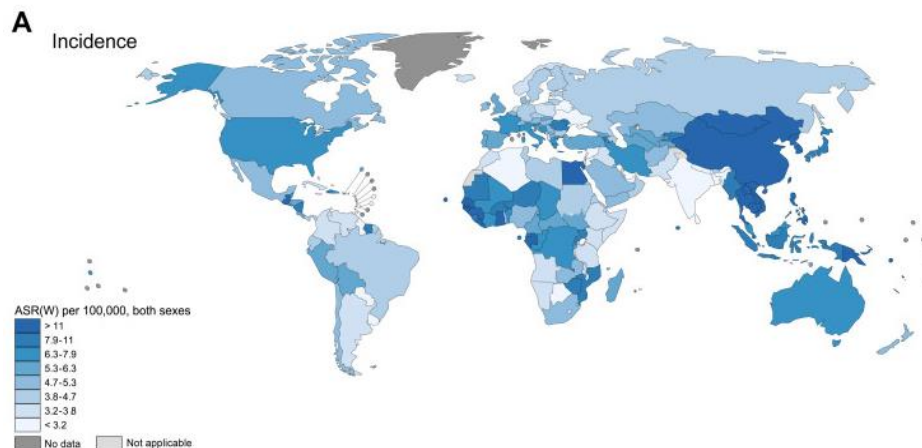
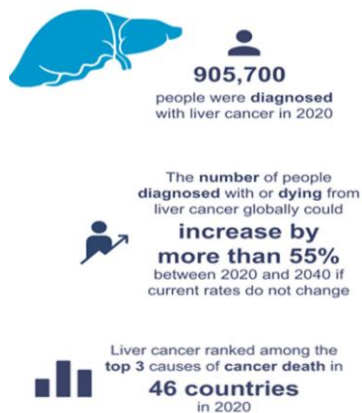
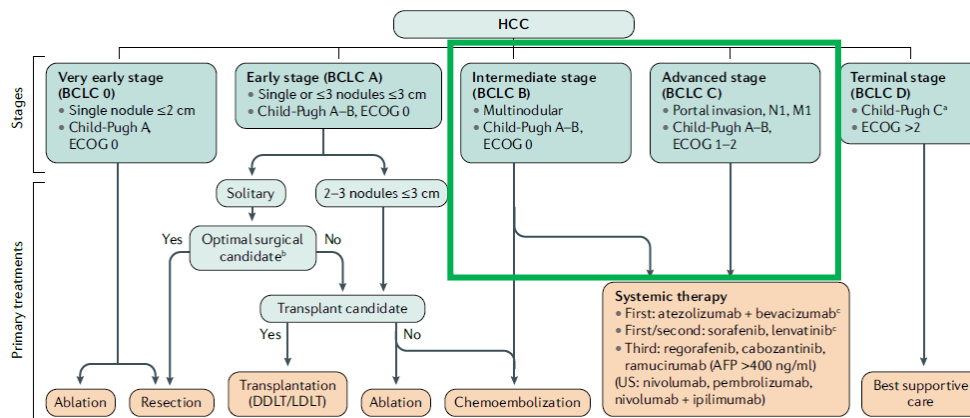
First-Line HCC Opportunity

First-line HCC is a Large and Uncrowded Market

TPST-1120's MoA and lead position offers a unique opportunity¹ to build a valuable program

| HCC | Incidence | 1L (treated) (BCLC B/C) |
|-------|-----------|----------------------------|
| US | 32,128 | 14,233 |
| EU5 | 33,995 | 15,499 |
| China | 324,012 | 205,053 |
| Total | 390,135 | 234,785 |

1L HCC is dominated by a single therapy
Even conservative market penetration
projections reveal significant value



TPST-1120 Phase 1 Data

Supports Expanded Oncology Franchise

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

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

Monotherapy

3+3 Design

TPST-1120 up to 600 mg BID

Combo with α PD-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 stable disease (SD) in late-stage patients with difficult-to-treat indications¹
 - 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

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

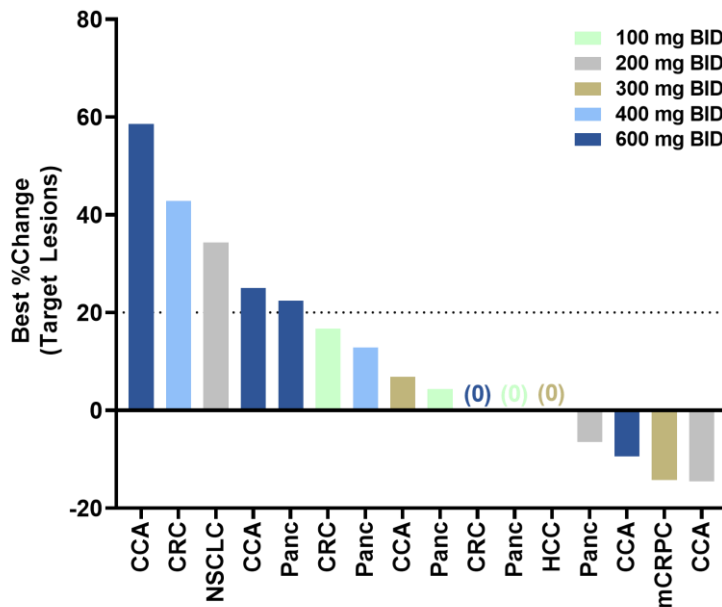
*Related to either TPST-1120 or nivolumab

- 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

Phase 1 TPST-1120 Activity Across Multiple Tumor Types

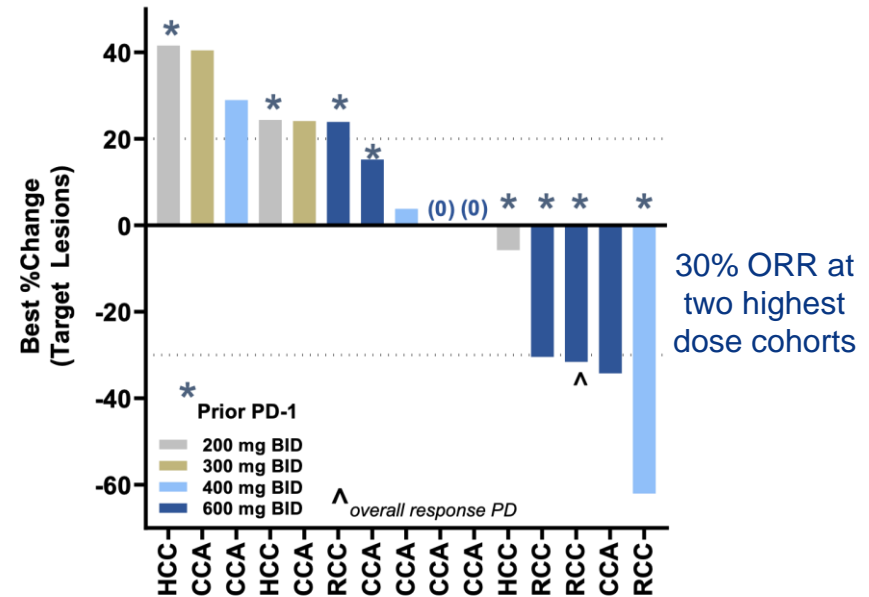
RECIST responses and disease control in difficult-to-treat, late-stage patient population

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



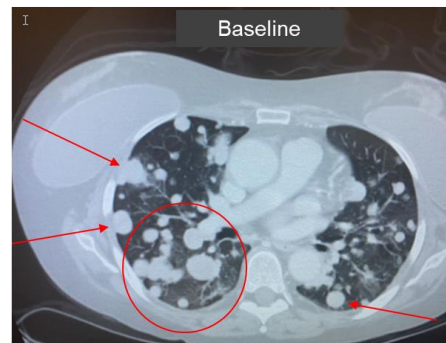
- Responses in patients with IO refractory (RCC) or IO non-responsive (CCA) indications
- All patients received approved α -PD1
- Responses in two highest dose cohorts

RCC Responses with TPST-1120 + Nivolumab

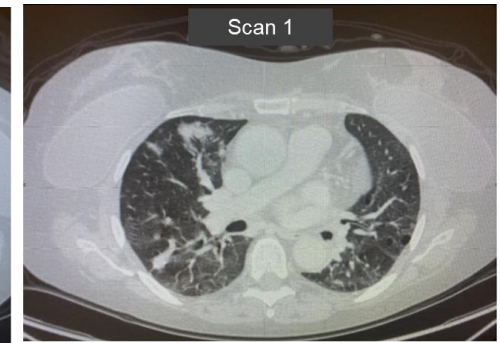
Two patients with IO-refractory, late-line, RCC experienced rapid RECIST responses

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



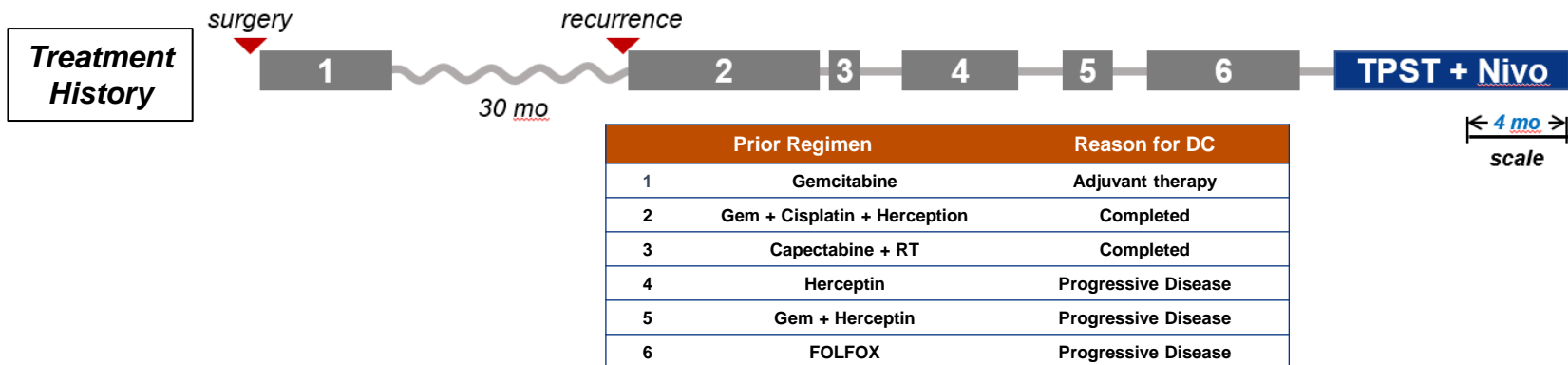
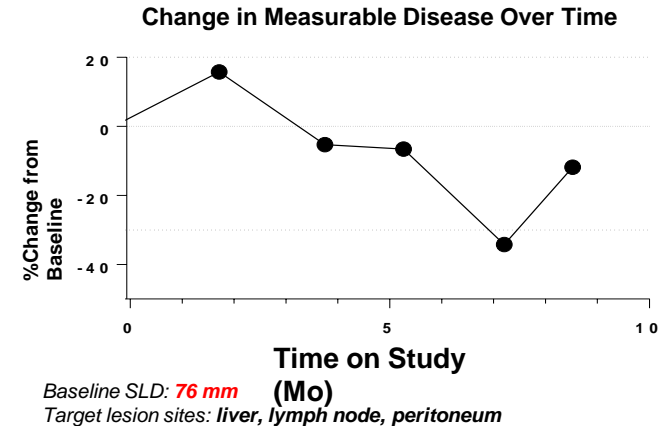
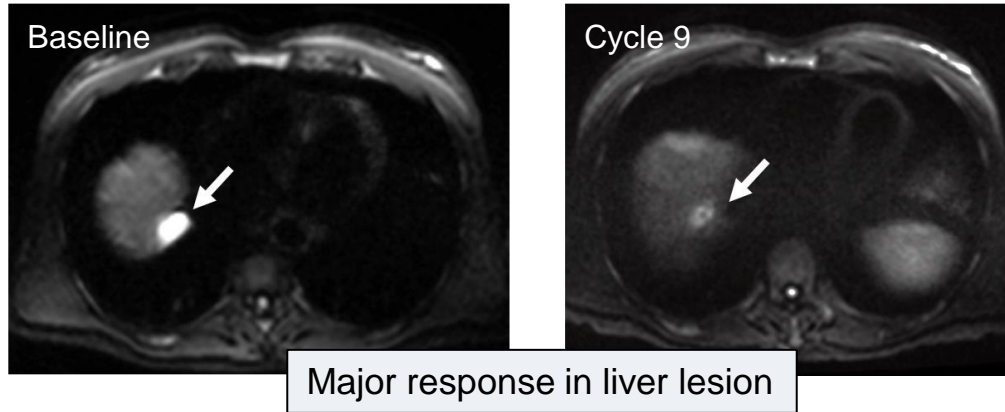
Subject 22-008

- 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 AE¹

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

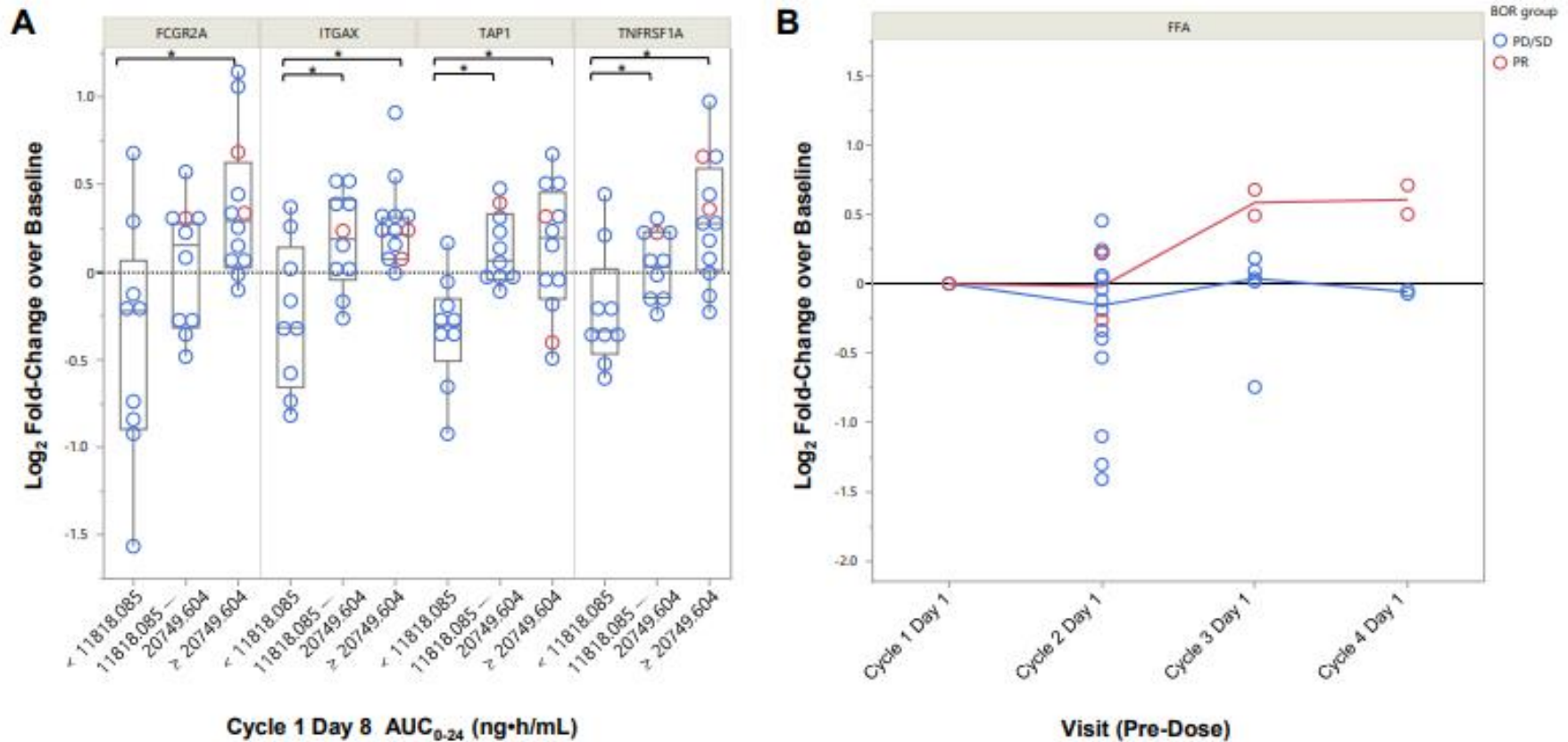
Cholangiocarcinoma Response with TPST-1120 + Nivolumab

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



TPST-1120 Induces Expression of Immune-Related Genes and Elevated Free Fatty Acids.

TPST-1120 exposure-dependent activity



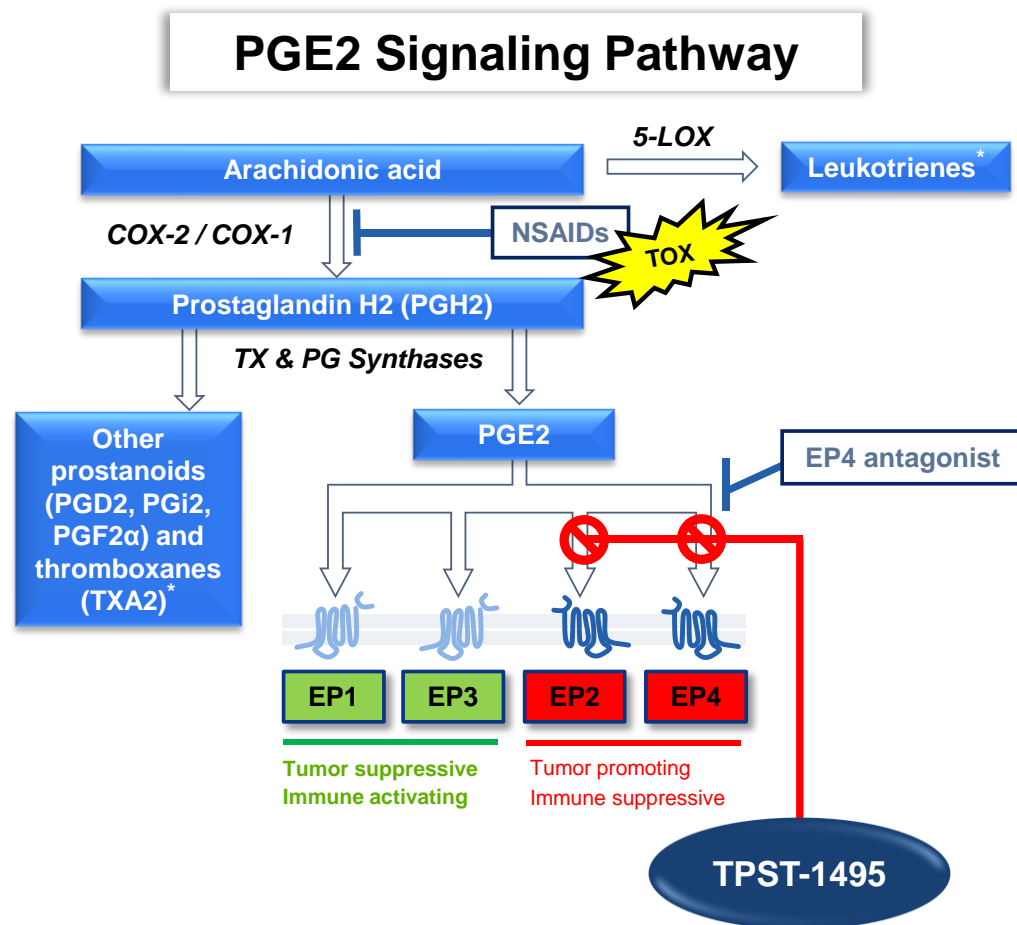
TPST-1495

First-in-Class Dual EP2/4 Antagonist

TPST-1495 is a First-in-Class¹ Dual EP2/EP4 PGE2 Receptor Antagonist

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

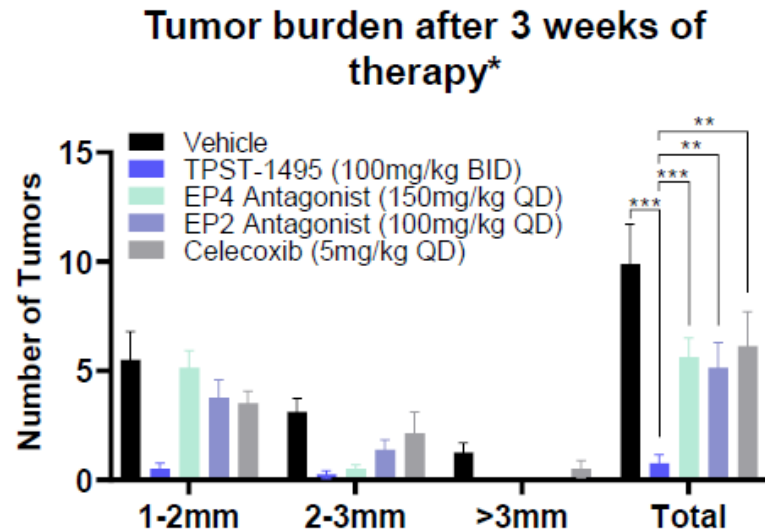
- Prostaglandin E₂ (PGE2) has both tumor *promoting* and tumor *suppressing* activity through its 4 receptors (EP 1-4)
 - NSAIDs prevent signaling through beneficial EP receptors and have toxicity
- TPST-1495 features
 - First in class, highly specific antagonist inhibits *only* the tumor promoting EP2 and EP4 receptors
 - Oral therapy
 - Nanomolar potency²
 - Targets *both* tumor cells and immune suppressive cells



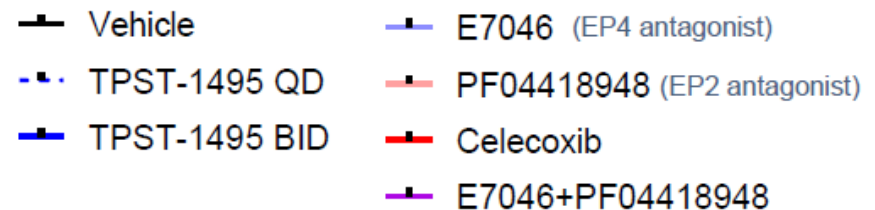
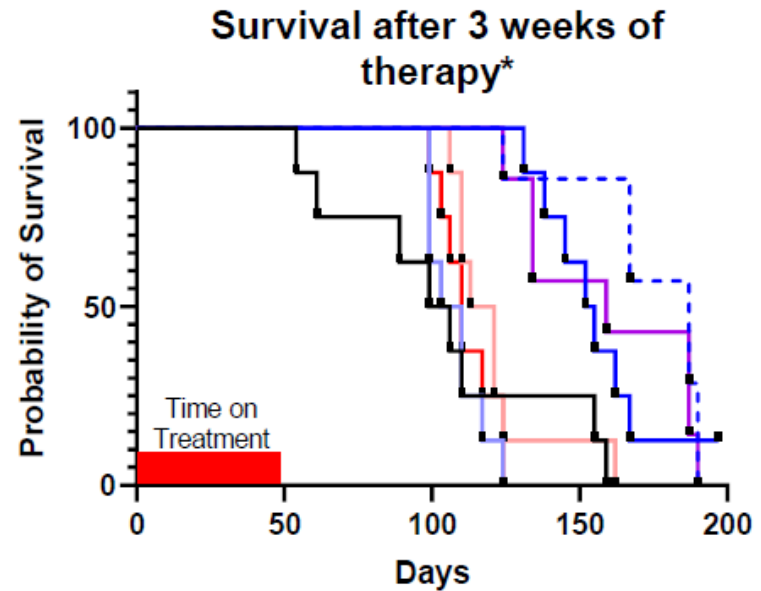
*Alterations in thromboxanes, prostacyclins and leukotrienes are associated with cardiovascular toxicity of NSAIDs

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 FAP



*Treatment initiated in 13-week-old mice.



TPST-1495 Program Summary

• ASCO June 2023 Phase 1 Poster

- 50 monotherapy, 24 in combination with pembrolizumab
- Predominantly MSS CRC (61%) & heavily pre-treated (median 4 priors for monotherapy)

Results highlighted in ASCO abstract:

- Manageable toxicity mono and combo – no MTD but QD schedule more tolerable than BID schedule (=RP2 schedule)
- Most common TRAEs of any grade and grade ≥ 3 were diarrhea (22%) and anemia (6%), respectively, for monotherapy and nausea (29%) and ALT/AST elevation and fatigue (4.2%), respectively, for combination
- DCR 43% (all SD) for monotherapy
DCR 43% (including 1 PR in MSS CRC) for combination
- PD activity observed in urine PGE2 metabolite and whole blood TNF α assay; endometrial patient with -22% tumor shrinkage had elevated COX-2 at baseline and increased CD8+ and GrB+TILs on treatment

ONGOING

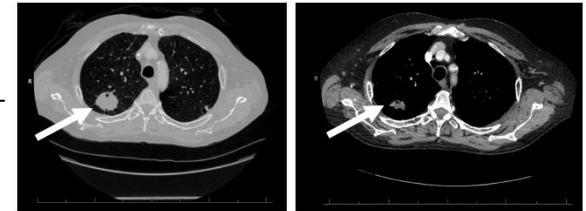
• Endometrial cancer expansion arm ongoing

• Familial Adenomatous Polyposis (FAP) Program

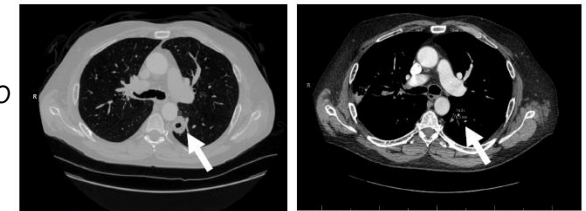
- No approved therapies for FAP (germline APC mutations)
- Strong clinical support for PGE2 MOA (COX-2s effective, Accelerated Approval for celebrex)
- Strong preclinical support for TPST-1495 based on Apc^{Min/+} model
- Working with FAP Consortium on an NCI-funded phase 2 study
- Pre-IND FDA meeting for FAP: received agreement that 1495 cancer IND tox package plus the Phase 1 safety data are sufficient to support 6 mo efficacy study in patients with FAP

ASCO poster highlighted CRC responder and long-duration endometrial patient with biomarker changes

- **4th line MSS-CRC** patient with confirmed RECIST Response (-38% BOR)



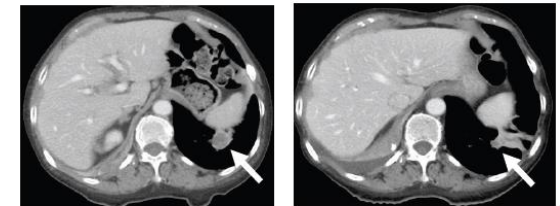
- Scans of lung met shrinkage were presented at ASCO



Baseline

Post-treatment

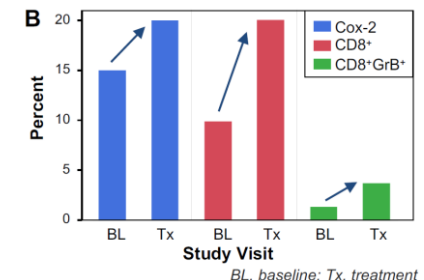
- **6th line MSS endometrial** patient with 22% reduction and >270 days on study



Baseline

Post-treatment

- Paired biopsies showed high baseline COX-2 expression & increased CD8+ and CD8+GrB+ infiltrate

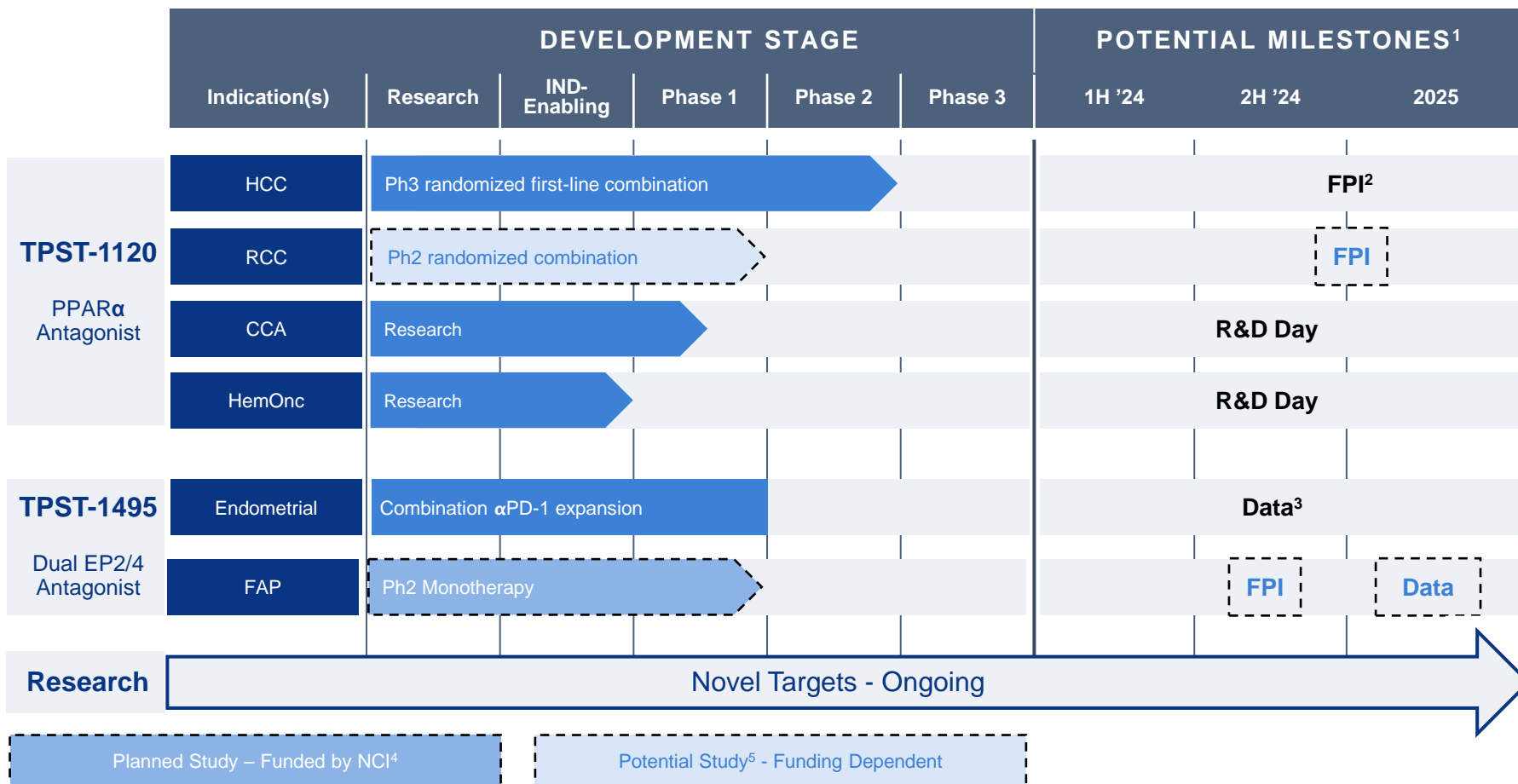


BL, baseline; Tx, treatment

Upcoming Milestones

Evolution to Pivotal Development in Large 1L HCC Indication

TPST-1120 has broad potential in HCC & beyond; optionality in TPST-1495 & earlier programs



"RCC" renal cancer; "HCC" hepatocellular carcinoma; "CCA" cholangiocarcinoma; "FAP" familial adenomatous polyposis. "ORR" Objective Response Rate; "PFS" Progression Free Survival; "FPI" First Patient In



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THERAPEUTICS

Company Overview

April 2024