TEMPEST

THERAPEUTICS

Company Overview

October 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 amezalpat[1] (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-Q filed by Tempest Therapeutics with the Securities and Exchange Commission for the quarter ended June 30, 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.

[1] Recommended International Nonproprietary Name (INN), April 22, 2024

Amezalpat (TPST-1120) OS Data Complete Positive Data Set
FDA Agreement on Phase 3

- ✓ **Amezalpat randomized 1L HCC data are superior to SoC arm**
  - New OS data shows six-month improvement with strong and stable HR (0.65)
  - Biomarker data further support dual MOA of TPST-1120
  - Large and growing commercial opportunity in HCC; positive data in RCC & CCA
- ✓ **Ownership and full control of diversified portfolio - strategic optionality**
- ✓ **Experienced team with proven track record**

Amezalpat Combination is Poised for Phase 3 Registrational Trial

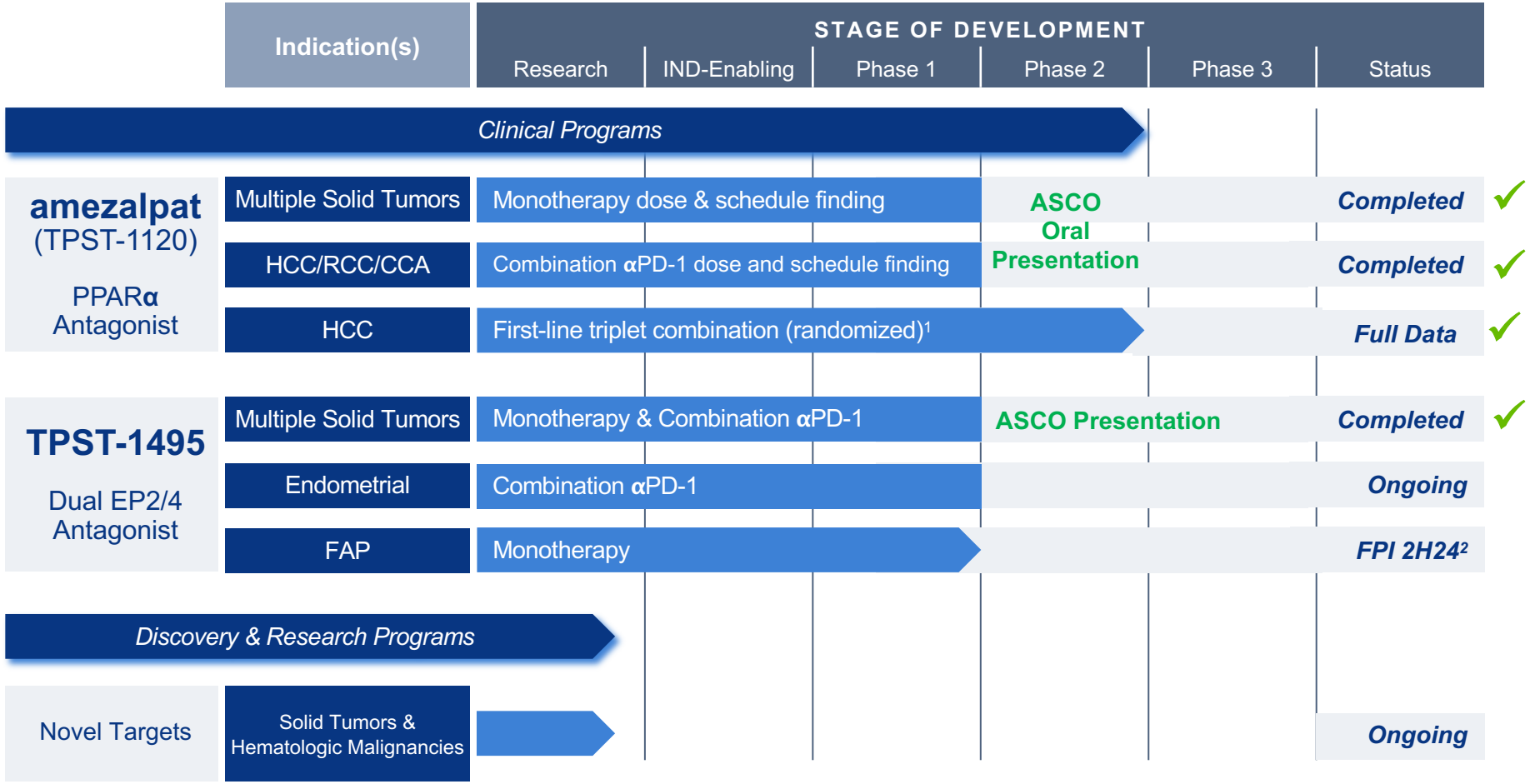
Survival benefit over SOC in full patient population and key subgroups, with similar safety profile to SoC alone

- ✓ 0.65 hazard ratio for OS – stable from topline through follow-up survival analysis
- ✓ Six-month improvement in median OS over control arm (21 months vs. 15 months)
- ✓ 20/40 patients remain in survival follow up in amezalpat arm vs. 9/30 in control
- ✓ Survival benefit maintained across key subpopulations, including PD-L1 negative
- ✓ Manageable safety profile similar to SOC
- ✓ FDA end-of-phase 2 completed with agreement on proposed pivotal study
- ✓ Oral therapy with potential market advantages

Data as of February 14, 2024. Hazard ratio was 0.59 at primary data analysis, ten months earlier than follow-up analysis.

First-in-Class Oncology Pipeline with Broad Potential

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



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"HCC" hepatocellular carcinoma, "RCC" renal cell carcinoma, "CCA" cholangiocarcinoma
First in class is dependent on FDA approval. [1] Pursuant to a collaboration with Roche; TPST retains all product rights. [2] Initial approval by the National Cancer Institute (NCI) received; awaiting final approval.

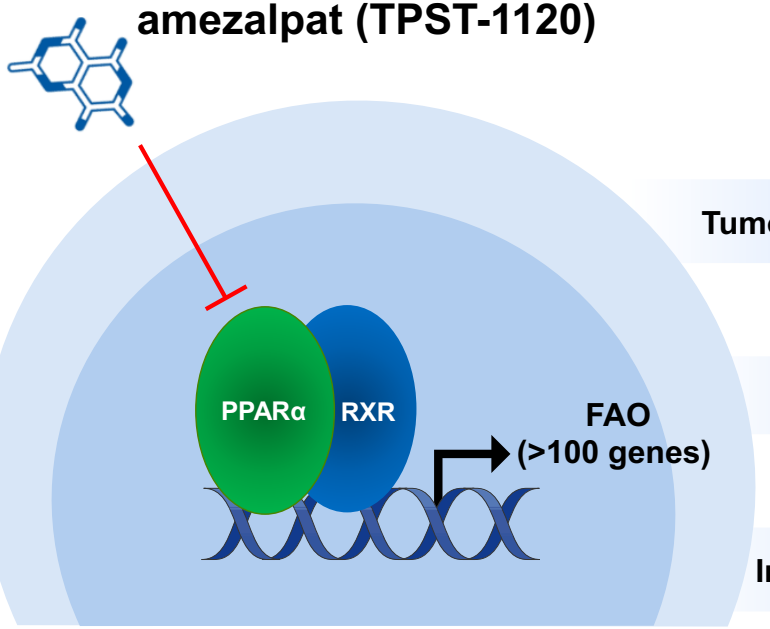
Amezalpat (TPST-1120)

First-in-Class PPARα Antagonist

Amezalpat (TPST-1120) in HCC: MOA Supports Indication & Combination Therapy

Original hypothesis: amezalpat will improve activity of anti-VEGF & ICI therapy - now supported by randomized Phase 2 data

HCC: Highest Expression of PPARα and FAO Genes



Tumor cell proliferation

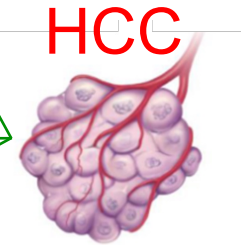
Angiogenesis

Immune suppression

Targets FAO-dependent tumors
(on-tumor activity)

Targets angiogenesis distinct from VEGF inhibitors
Combine with Bev

Targets FAO-dependent immune suppressor cells
Combine with ICI



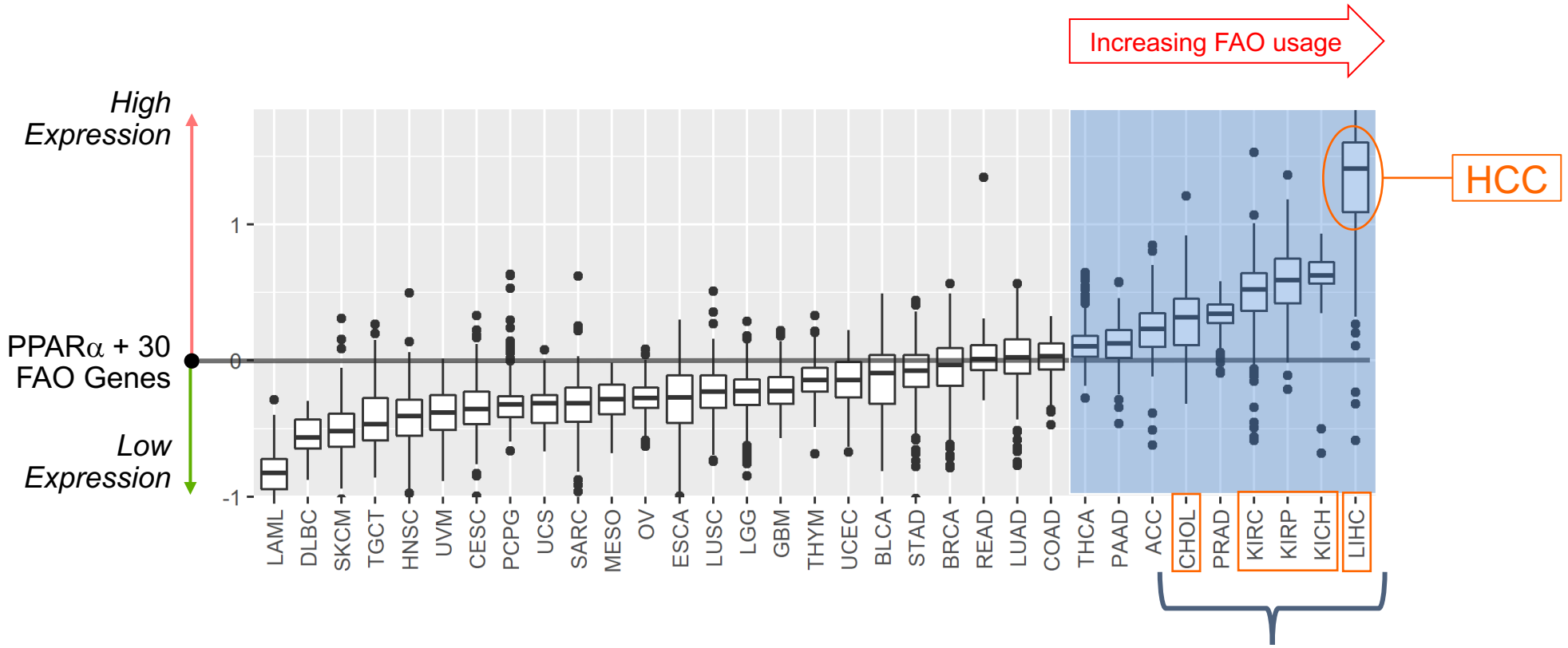
PPARα: Peroxisome Proliferator-Activated Receptor alpha

[1]First-in-Class status is dependent on FDA approval

"FAO" = fatty-acid oxidation, "VEGF" = vascular endothelial growth factor, "ICI" = immune checkpoint inhibitor

FAO-Dependent Tumors Inform Development Strategy

TCGA-based analysis of tumor metabolic gene expression profiles

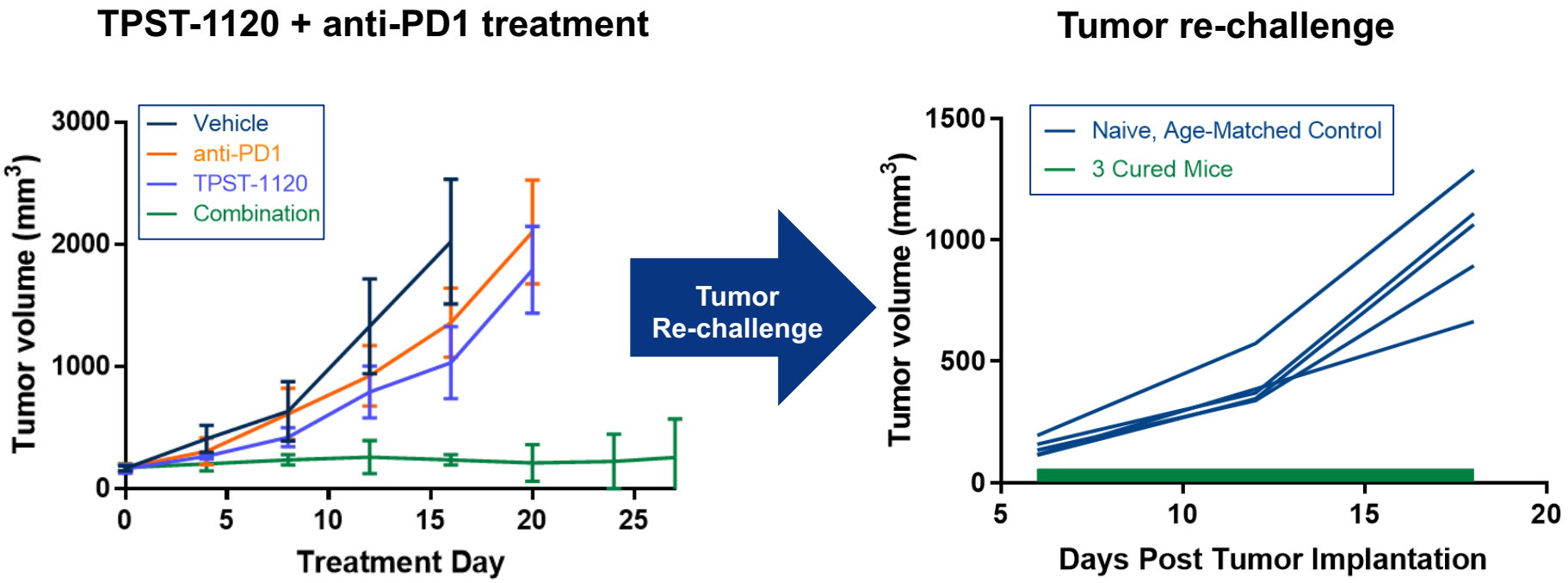


Positive patient data in HCC, RCC, and cholangiocarcinoma

Source: https://www.cancer.gov/ccg/research/genome-sequencing/tcga

Durable Responses in Combination with α-PD-1

MC38 colorectal cancer tumor model, C57BL/6 immunocompetent mice



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

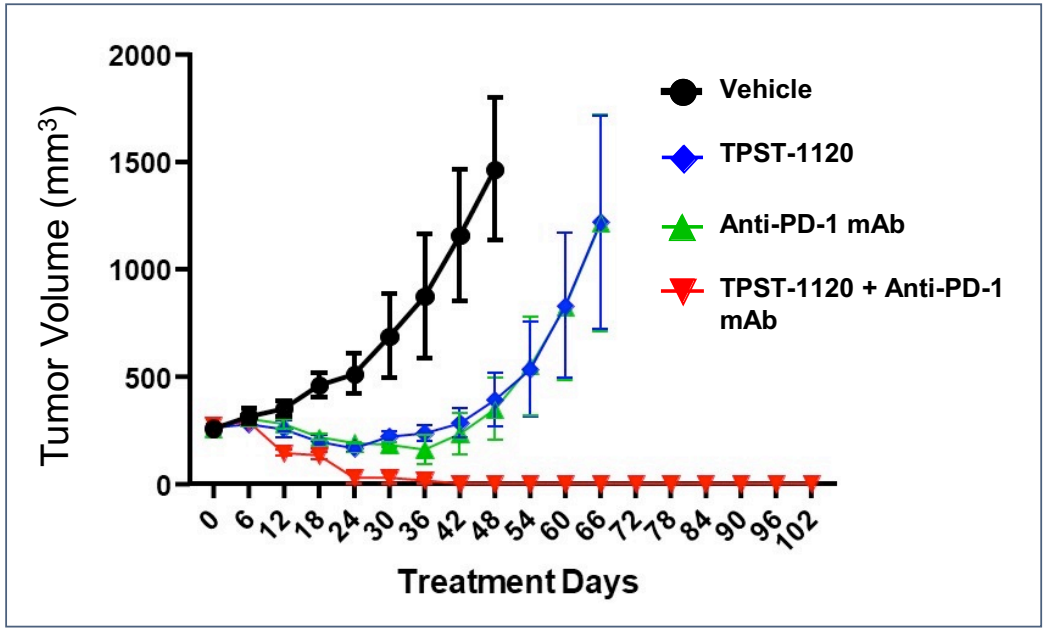
Source: Dipak Panigrahy, Harvard

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[1,2]
- PPARα 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*



[1]Morita et al Cancers 2023. [2]de Galarreta et al Cancer Discov 2019;9:1124–41

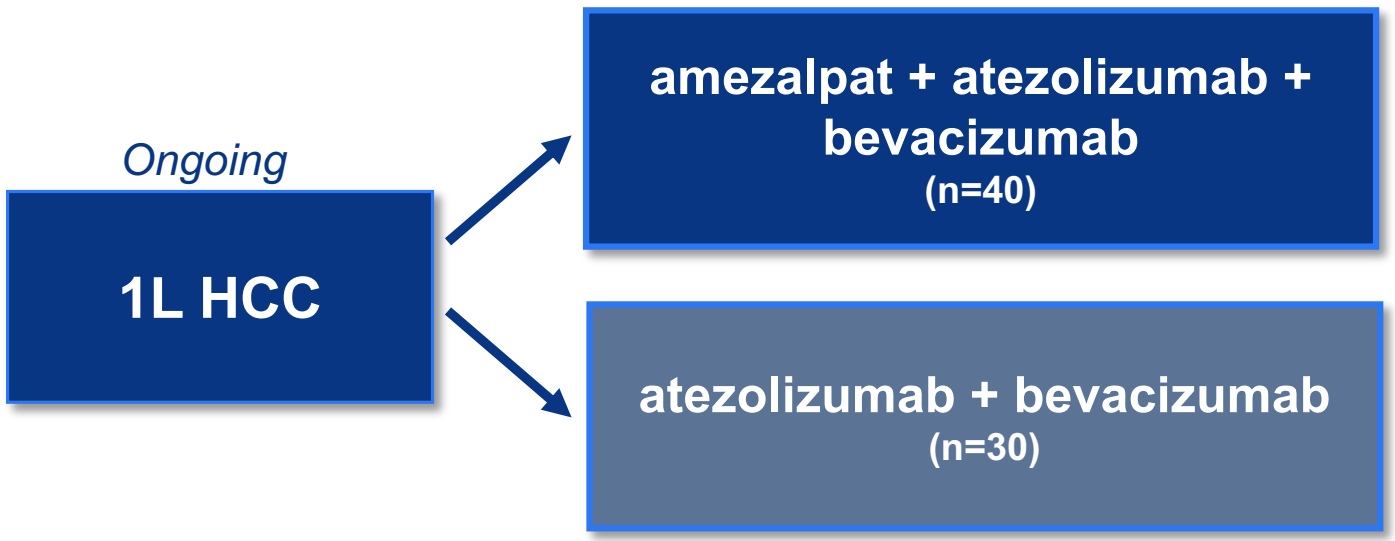
Amezalpat (TPST-1120) Randomized Clinical Data

First-Line HCC Compared to SoC

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

Positive Global Randomized Phase 2 result positions Tempest for pivotal study

HCC: Highest Expression of PPARα and FAO Genes



- SoC 1L regimen +/- TPST-1120
- Ongoing multi-arm global randomized study[1]
  - 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

[1] Morpheus HCC study in collaboration with Roche (NCT04524871) – Tempest retains all product rights; IE criteria based on pivotal IMbrave 150

"1L" = front-line, "ORR" = objective response rate, "SoC" = Standard of Care, "PFS" = progression-free survival, "OS" = overall survival

Balanced Demographics and Baseline Characteristics

No statistically significant differences, although multiple numerical differences favor the SoC 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, 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 disease[1]

[c] A number of recent studies have reported that baseline NLR is predictive of ORR and/or OS in HCC with atezo + bev regimen[2]. [d]25 subjects PD-L1 evaluable; [e]39 subjects PD-L1 evaluable

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[1] Cheng AL, et al. Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. Journal of Hepatology 2022 vol. 76 862–873; Espinoza M, et al. Disease Etiology and Outcomes After Atezolizumab Plus Bevacizumab in Hepatocellular Carcinoma: Post-Hoc Analysis of IMbrave150 [published online ahead of print, 2023 Mar 7]. Gastroenterology. 2023;S0016-5085(23)00234-2. [2] Eso, Y. et al. Pretreatment Neutrophil-to-Lymphocyte Ratio as a Predictive Marker of Response to Atezolizumab Plus Bevacizumab for Hepatocellular Carcinoma. Curr. Oncol. 2021, 28, 4157–4166.; Chon YE, et al. Predictive biomarkers of survival in patients with advanced hepatocellular carcinoma receiving atezolizumab plus bevacizumab treatment. Cancer Medicine. 2023;12:2731–2738

Amezalpat (TPST-1120) Arm Improves All Efficacy Endpoints vs. SoC Control

Primary Global Regulatory Endpoint

	atezo/bev N=30	TPST-1120 + atezo/bev N=40
OS **HR 0.65**	15m	**21m**
PFS **HR 0.8**	Median 4.27m (2.8, 7.3)	**7m** (5.6, 13.8)
Confirmed ORR (ITT population)	13.3%	**30%**
PD-L1 negative Confirmed ORR	7%	**27%**
β-catenin mutation Confirmed ORR	N/A[1]	**43% (100% DCR)**

Consistent Improvement Across All Endpoints

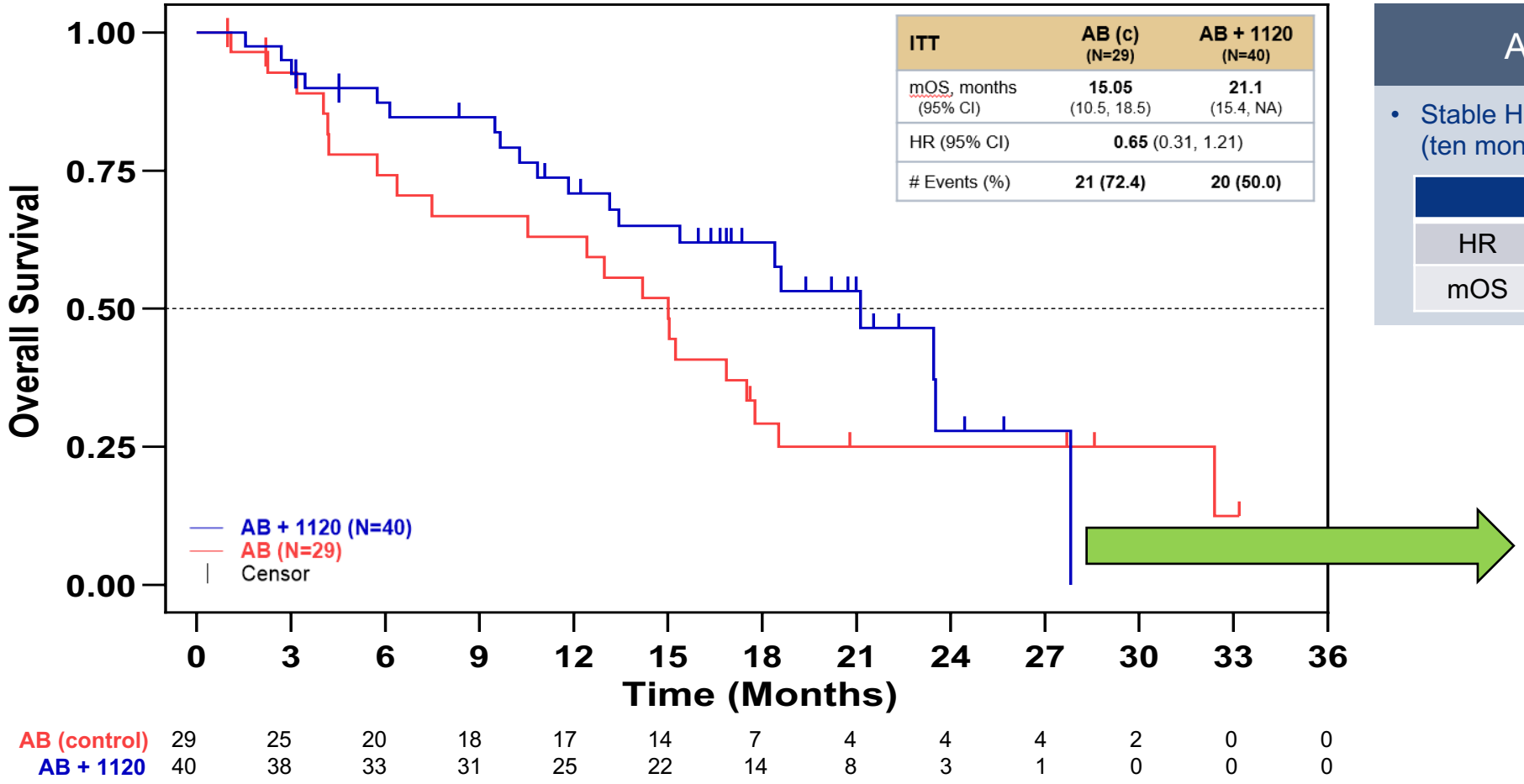
- **Biomarkers and pharmacodynamic data support MOA of amezalpat**
  - Consistent with mechanism, amezalpat improves activity of atezo+bev in PD-L1 negative and immune desert/excluded phenotype compared to atezo+bev alone
  - β-catenin activation and FAO upregulation improve activity in amezalpat arm
- **Manageable safety profile - no new signal**

February 14, 2024 data update; [1] Data not provided by Roche.

"HR" = Hazard Ratio

Superior OS in Amezalpat (TPST-1120) Arm vs. Atezo-Bev Control

- **HR 0.65** - early and persistent separation of survival curves
- **Six-month improvement in mOS** with 50% of amezalpat arm patients still in survival follow-up[1]



ITT	AB (c) (N=29)	AB + 1120 (N=40)
mOS, months (95% CI)	15.05 (10.5, 18.5)	21.1 (15.4, NA)
HR (95% CI)	0.65 (0.31, 1.21)	
# Events (%)	21 (72.4)	20 (50.0)

A Closer Look at HR

- Stable HR compared to April 2023 data cut (ten months earlier)

	Apr '23	Feb '24
HR	0.59	0.65
mOS	NR vs. 15	21 vs 15

20/40 patients in **amezalpat arm** remain in survival follow up vs. 9/30 on atezo-bev control arm

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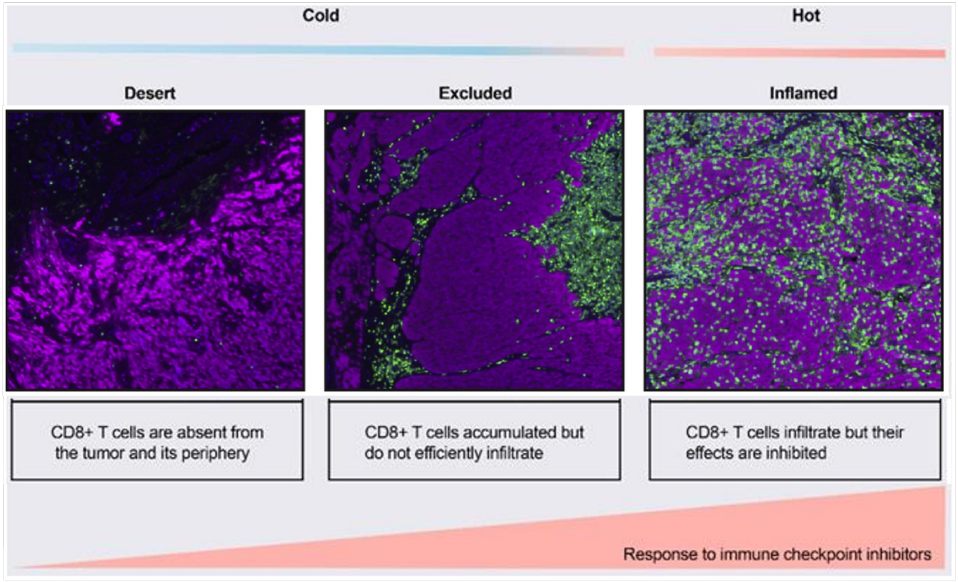
[1] February 14, 2024 data cut. *Elongated censor symbols are permanently censored subjects*

"mOS" = median overall survival, "AB" = atezolizumab + bevacizumab, "CI" = confidence interval

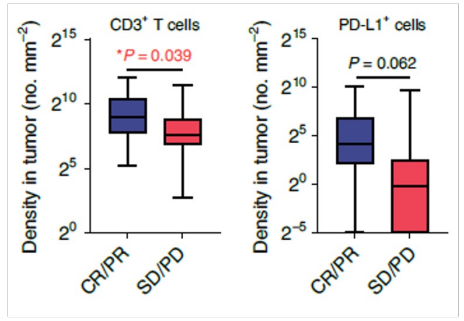
Amezalpat (TPST-1120) Improves ORR in Two Difficult Sub-populations

β-Catenin (CTNNB1) mutants and PD-L1 negative HCC patients both responded to TPST-1120 therapy

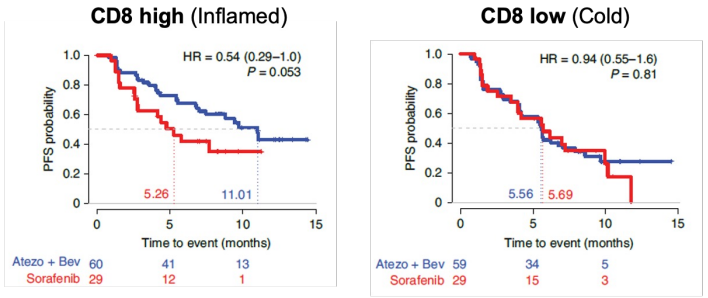


Tumor images representing 3 patterns of T cell infiltration visualized by CD3+ T cells (green) and a tumor marker (magenta). Van der Woude Trends in Cancer 2017.

ORR Atezo/Bev



PFS

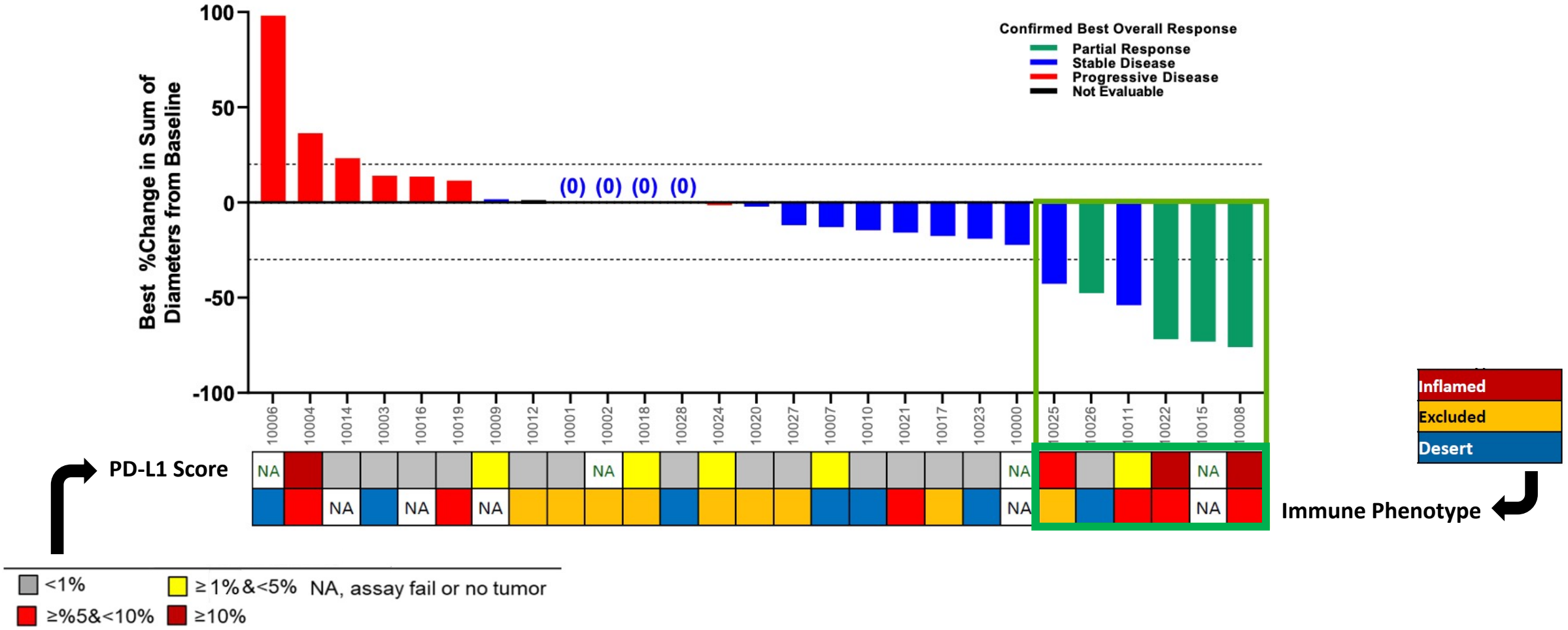


- The majority (60-70%) of HCC tumors are non-inflamed and/or PD-L1 negative [1,2,3]
- *CTNNB1* mutations in HCC are associated with non-inflamed tumors and ICI resistance[4,5]
- Reduced atezo/bev activity was observed in HCC patients with immune cold and PD-L1 negative tumors[6]

[1]Sia et al Gastroenterology 2017. [2]Mou et al J Gastroenterol Hepatol 2021. [3]Wang et al Annals of Oncology 2020 [4]Morita et al Cancers 2023. [5]de Galarreta et al Cancer Discov 2019;9:1124–41 [6]Zhu et al Nat Med 2022.

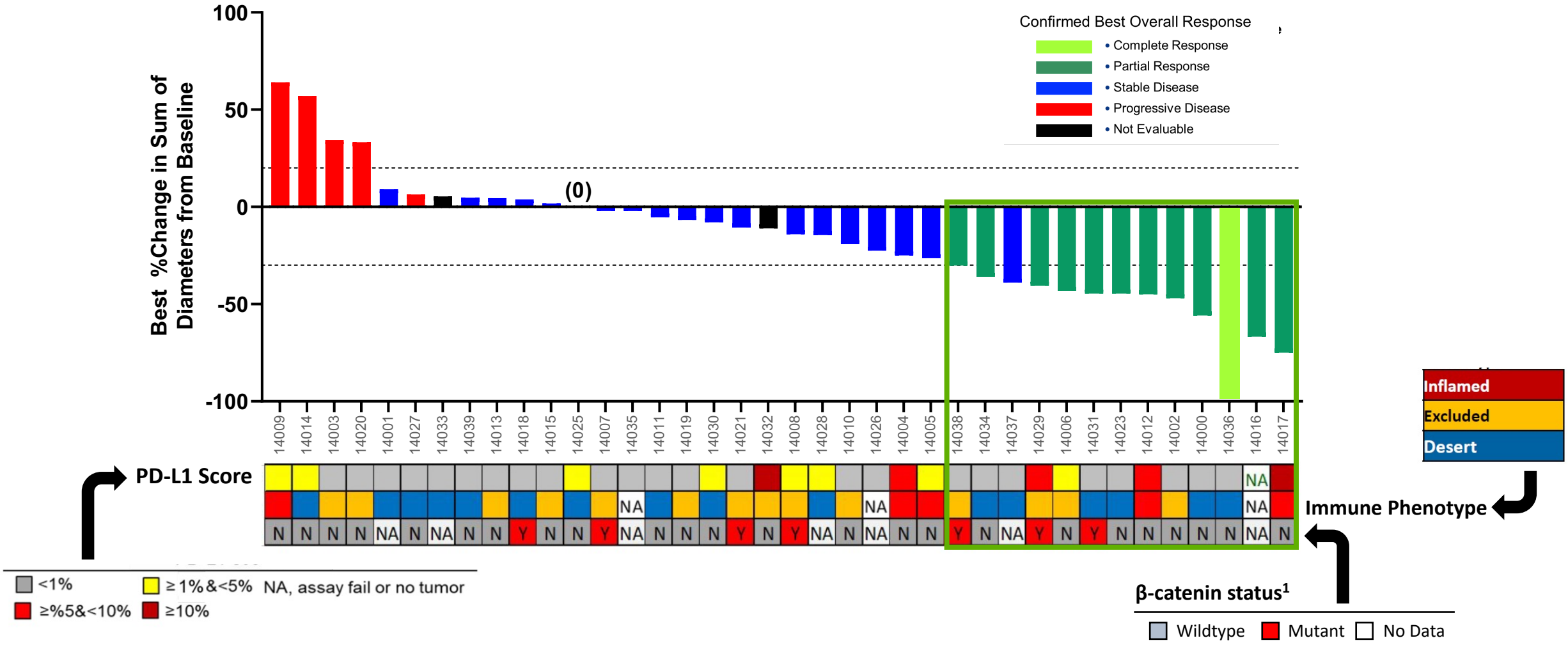
AB SoC Control Arm Responses Enriched for PD-L1+ and Hot Tumors

Atezo + Bev biomarker associations



Amezalpat Responses Across the Board: Cold, Hot and β-catenin$^{mut\ \&\ wt}$ Tumors

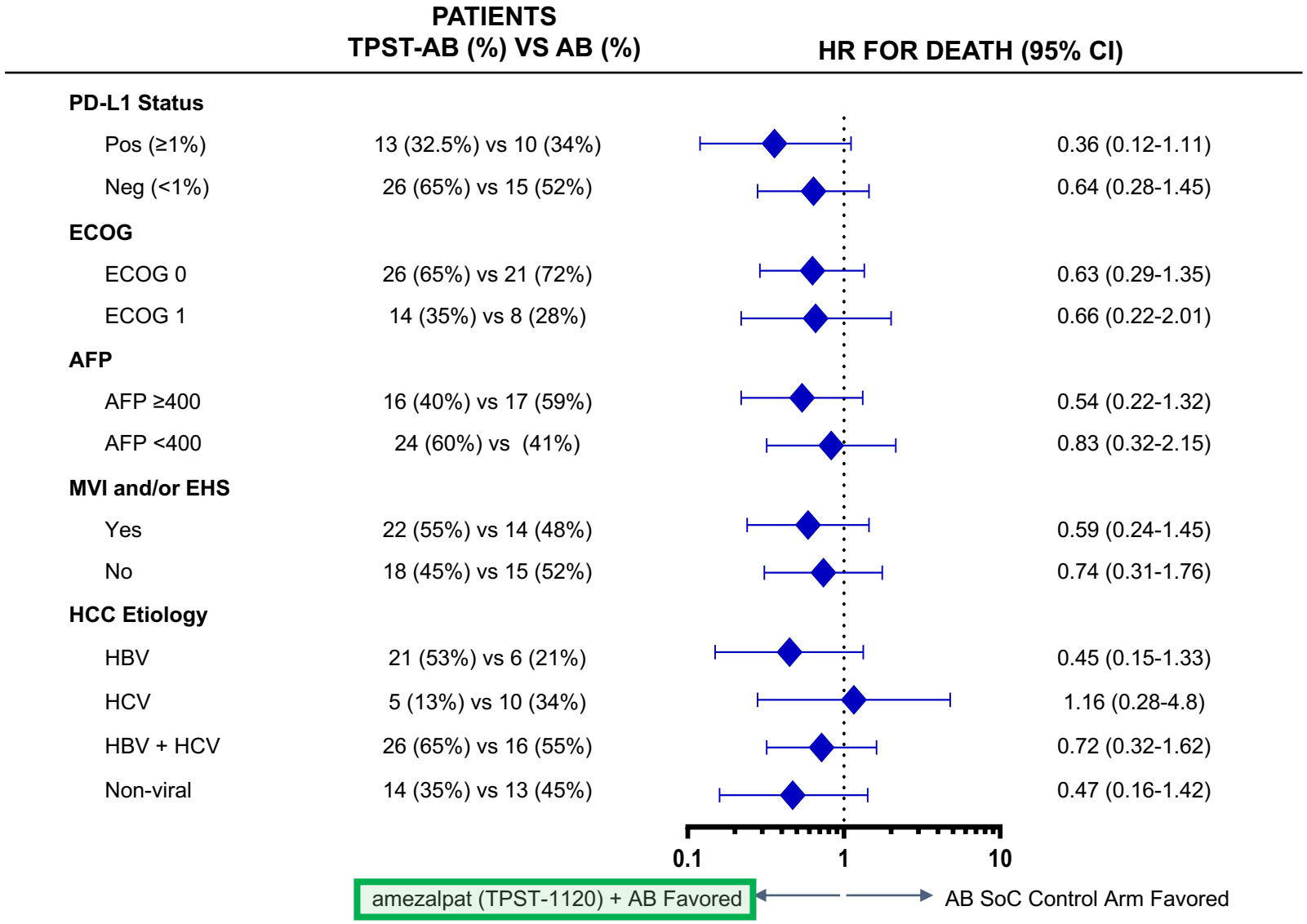
RECIST Complete Response in a PD-L1 negative, immune excluded and β-catenin (CTNNB1^{wt}) tumor



Primary data cut, per protocol - April 20, 2023

[1] CTNNB1 mutation measured

Overall Survival Benefit Maintained Across Key Subpopulations

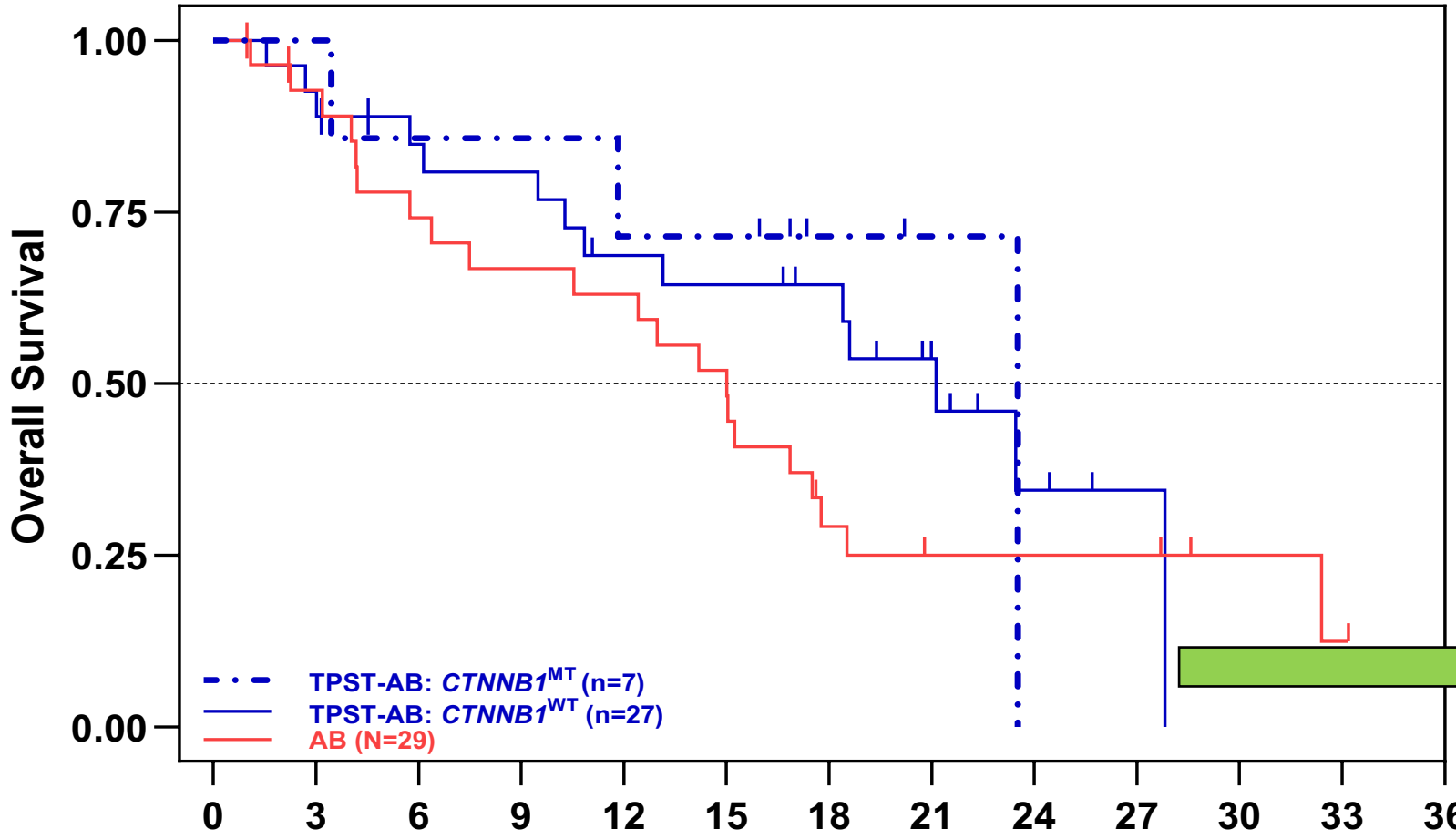


February 14, 2024 data cut

"AFP" = alpha fetoprotein, "MVI" = microvascular invasion, "EHS" extrahepatic spread

Overall Survival in Amezalpat (TPST-1120) β-catenin Patients vs. Control

Further support for development strategy in overall population independent of β-catenin (CTNNB1) status



TPST-1120 Arm

	CTNNB1^{MT} (n=7)	*CTNNB1*^{WT} (n=27)	AB (c) (N=29)
mOS, months (95% CI)	**23.5** (11.8, NA)	**21.1** (13.1, NA)	**15.0** (10.5, 18.5)
HR (95% CI) TPST-AB (MT) vs AB		**0.65** (0.34, 1.27)	
HR (95% CI) TPST-AB (WT) vs AB		**0.51** (0.19-1.32)	
# Events (%)	**3 (42.8)**	**14 (51.9)**	**21 (72.4)**

20/40 patients in **amezalpat/TPST-1120 arm** remain in survival follow up vs. 9/30 on atezo-bev control arm

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February 14, 2024 data cut.

Elongated censor symbols are permanently censored subjects

Manageable Safety Profile Consistent with MOA and Phase 1 Data

Amezalpat combination's safety profile is similar to AB SoC control arm

Patients with Event, n (%)	Atezo + Bev (N=29)	1120 + Atezo + Bev (n=40)
Grade 1 or 2 Severity TEAE	7 (24.1)	12 (30.0)
Grade ≥ 3 TEAE	22 (75.9)	28 (70)
Treatment-Related SAE*	7 (24.1)	10 (25.0)
Grade 5 TEAE	4 (13.8)	5 (12.5)
Grade 5 Treatment-Related AE	2 (6.9)	-
Any TEAE Leading to Drug Interruption/Dose Reduction^,†	6 (20.7)	6 (15.0)
Any TEAE Leading to Drug Withdrawal^	4 (13.8)	5 (12.5)

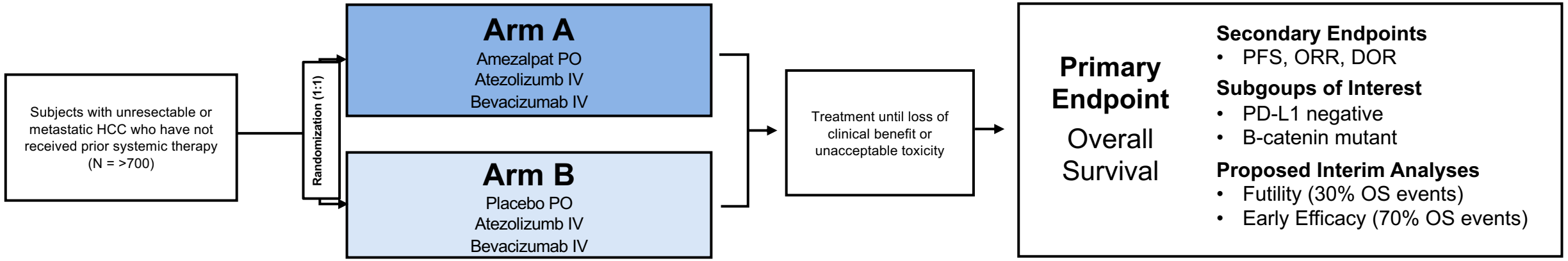
**Related to any drug*
^Any drug
†One subject dose reduced TPST-1120. Dose reductions not applicable to AB
Fatal TEAEs in AB arm: Aspiration, COVID-19, Oesophageal varices haemorrhage (related), Upper gastrointestinal haemorrhage (related)
Fatal TEAEs in TPST-AB arm: Acute kidney injury, cerebrovascular accident, diverticulitis, Fournier's gangrene, Oesophageal adenocarcinoma
Data as of Feb 14, 2024

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

Data as of April 20, 2023

Pivotal Phase 3 Study Design – End of Phase 2 FDA Meeting Complete

- Replicates positive Phase 2 study with additional size & power – increases probability of repeating Phase 2 result with regulatory statistical significance
- Agreement with FDA on all major aspects of Phase 3 design
- Planned analyses that could shorten timeline; Phase 2 data are stronger than required to win



Stratification factors:[1]

- Geographic region (Asia excluding Japan vs. rest of world)
- MVI and/or EHS (yes vs. no)
- Baseline AFP (< 400 vs. ≥ 400 ng/mL)
- Baseline ECOG PS (0 vs. 1)

Study Assumptions:

- 90% power
- 2-sided 5% alpha
- Critical hazard ratio[2] of **<.805** for primary efficacy and **<.729** for early efficacy (compare to **.65** in Phase 2)
- Control arm assumption based on longer historical value, as opposed to shorter Phase 2 & RW data
- 1:1, >700 subjects

[1] Under consideration and likely, although factors may change in final protocol. [2] Minimal hazard ratio for statistical significance

Amezalpat Combination is Poised for Phase 3 Global Registrational Trial

Survival benefit over SOC in full patient population and key subgroups, with similar safety profile to SoC alone

- ✓ 0.65 hazard ratio for OS – stable from topline through follow-up survival analysis
- ✓ Six-month improvement in median OS over control arm (21 months vs. 15 months)
- ✓ 20/40 patients remain in survival follow up in amezalpat arm vs. 9/30 in control
- ✓ Survival benefit maintained across key subpopulations, including PD-L1 negative
- ✓ Manageable safety profile similar to SOC
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Data as of February 14, 2024. Hazard ratio was 0.59 at primary data analysis, ten months earlier than follow-up analysis.

First-Line HCC Opportunity

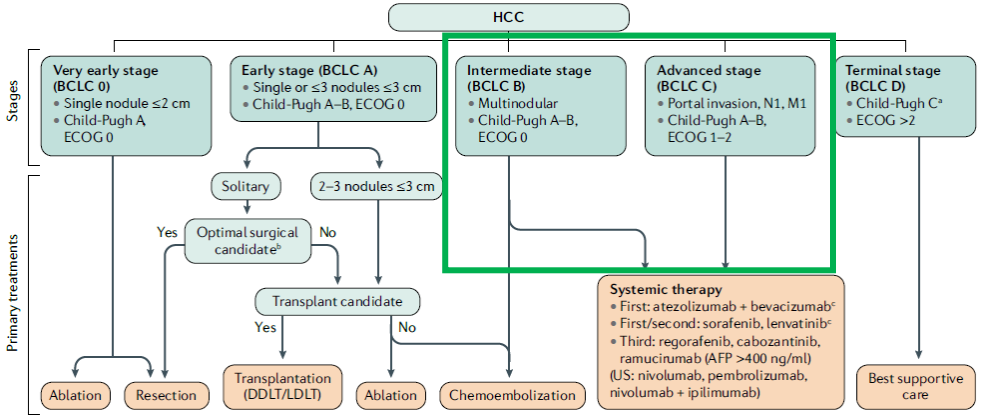
Proposed Phase 3 Design and Market

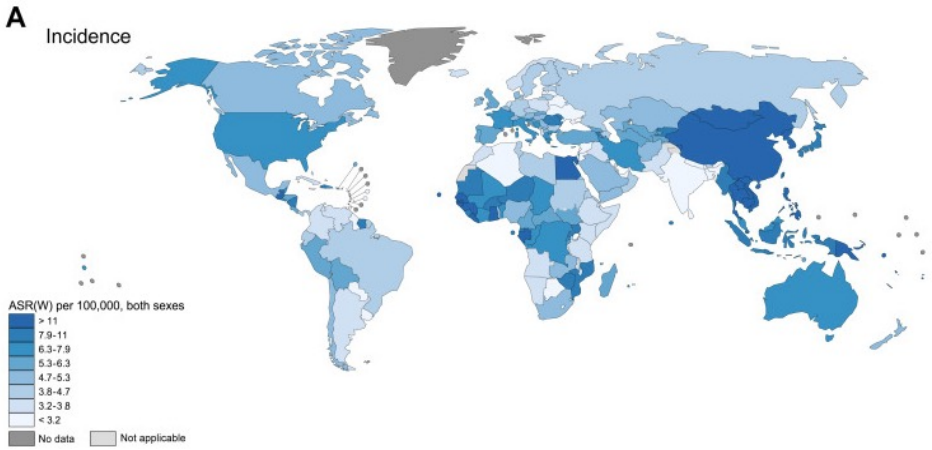
First-Line HCC is a Large and Uncrowded Market

Amezalpat's MoA and lead position offers a unique opportunity[1] 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





[1] To the company's knowledge, TPST-1120 is the latest stage and only PPARα antagonist in clinical development

Rumgay, H., et. al. "Global burden of primary liver cancer in 2020 and predictions to 2024," Journal of Hepatology, Vol. 77, Issue 6, pg: 1598-1606 (2022). Llovet, J.M., Kelley, R.K., Villanueva, A. et al. Hepatocellular carcinoma. Nature Review Dis Primers 7, 6 (2021). https://www.roche.com/investors/events/pharma-day-2023#:~:text=Roche%20has%20hosted%20its%20Pharma%20Day%20on%2011th%20September%202023%20in%20London. Accessed Jan 2024.

TPST-1120 Phase 1 Data

Supports Expanded Oncology Franchise (RCC, CCA)

ASCO 2022 - Oral Presentation

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 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 stable disease (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

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[1] Oral presentation at ASCO 2022

TPST-1120 Has A Manageable 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

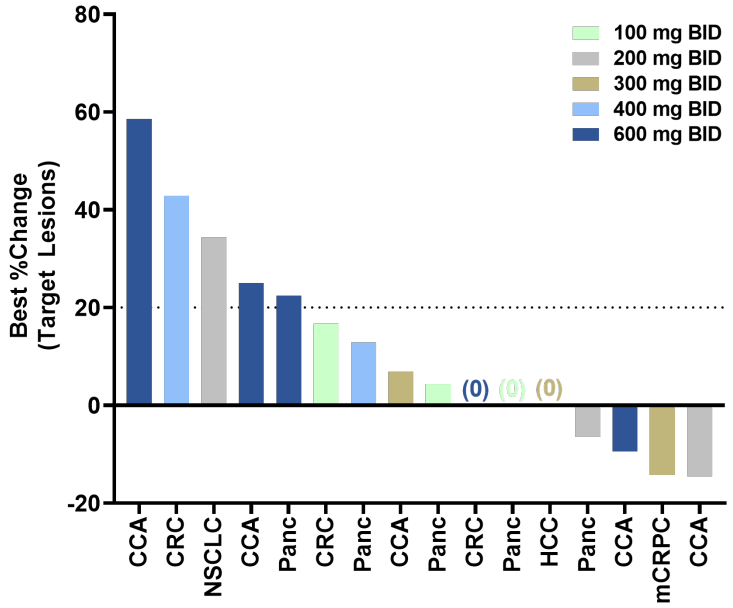
*Related to either TPST-1120 or nivolumab

- TPST-1120 showed manageable 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

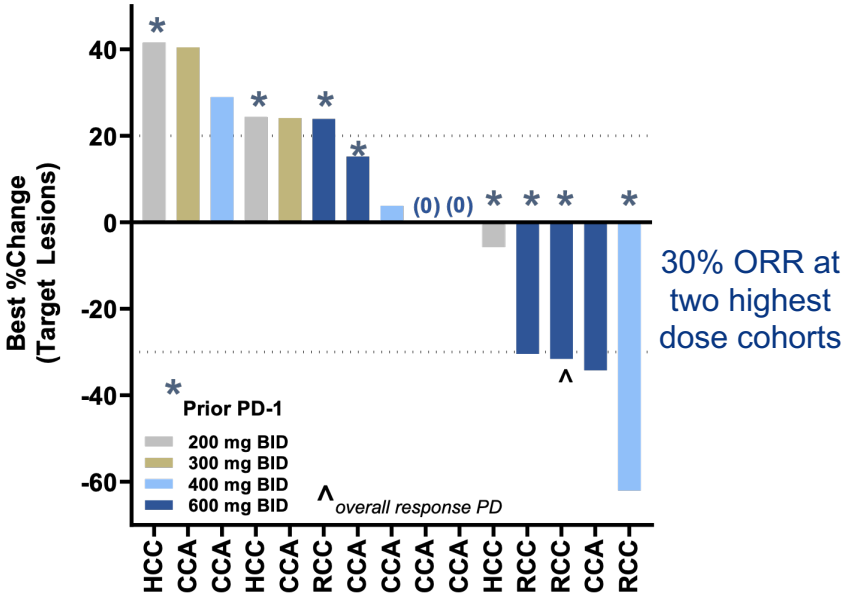
RECIST responses and disease control in difficult-to-treat, late-stage patient population

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



30% ORR at two highest dose cohorts

- 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

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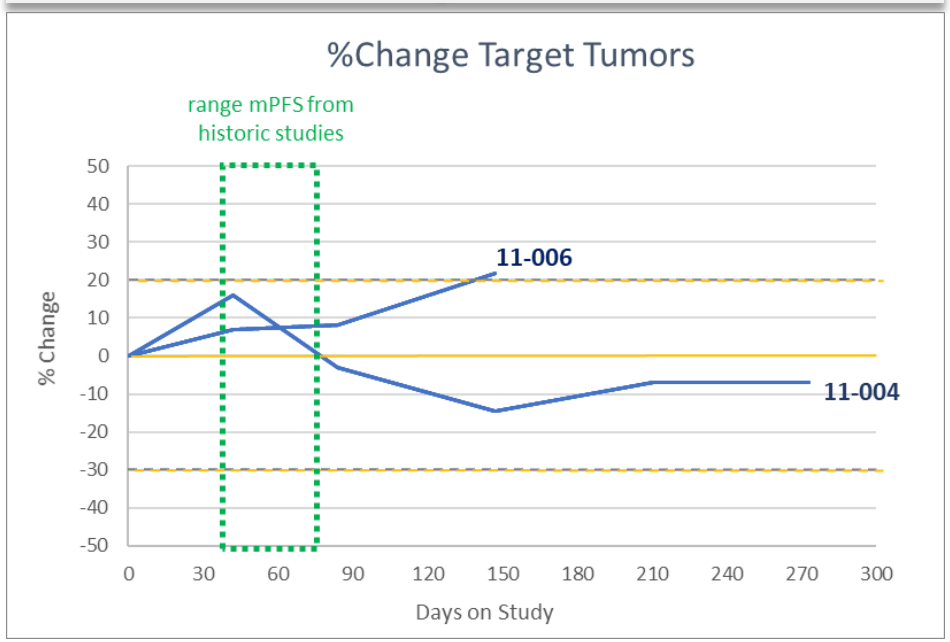
Response evaluable patients include pts with a postbaseline scan or discontinued treatment due to disease progression. DCR, disease control rate = complete response + partial response + stable disease. April 15, 2022 data cut. [1] Median three prior lines of therapy

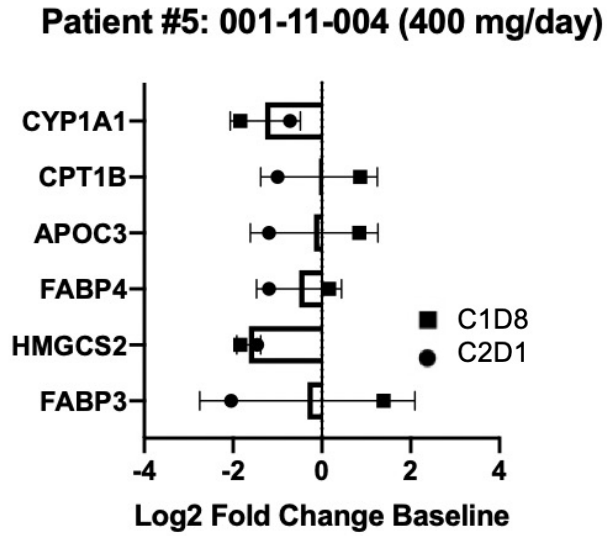
Monotherapy Tumor Control in Late-Line Cholangiocarcinoma

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 partially monitored

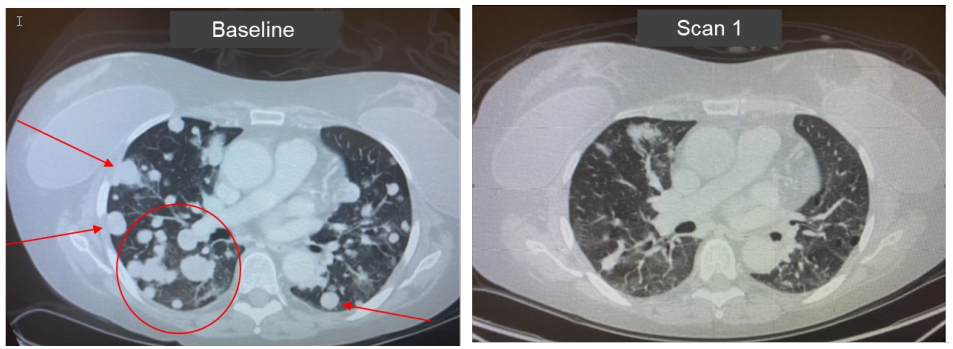
RCC Responses with TPST-1120 + Nivolumab

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 AE[1]

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

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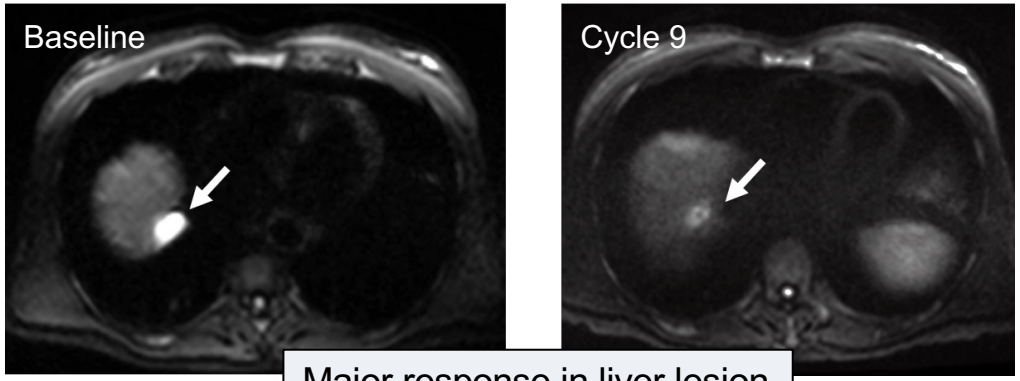
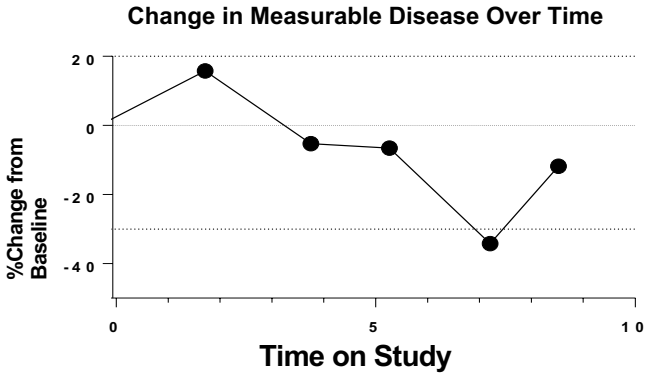
[1] Was unable to restart treatment; disease progressed while off treatment

Cholangiocarcinoma Response with TPST-1120 + Nivolumab

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

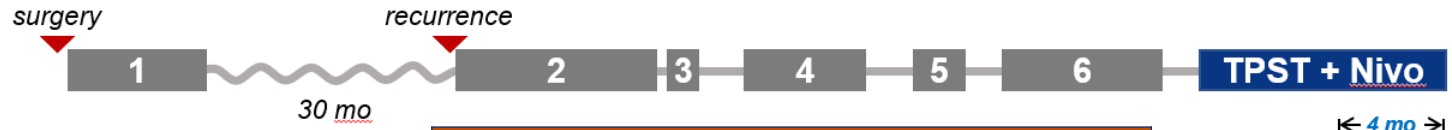


Major response in liver lesion



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

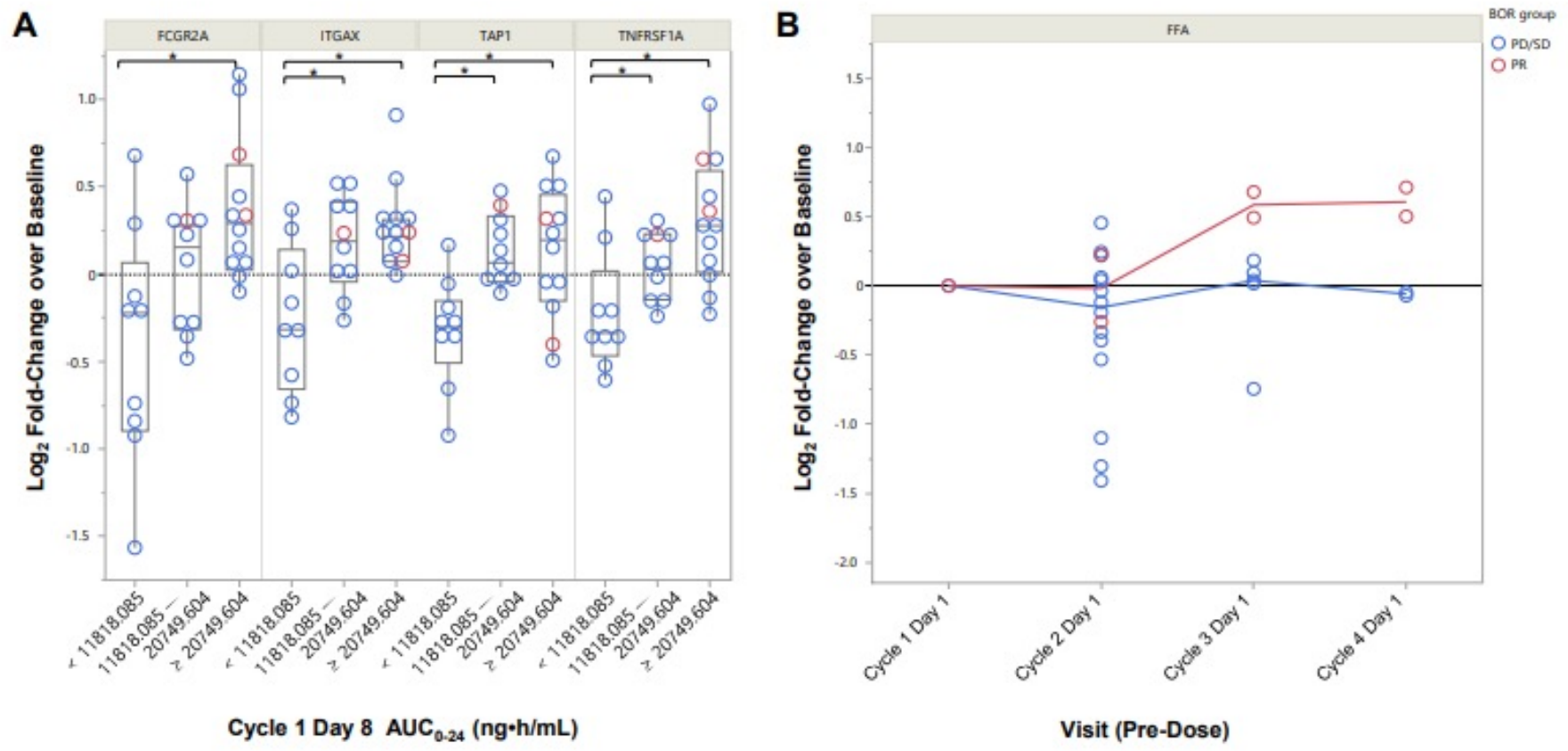
Treatment History



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

TPST-1120 exposure-dependent activity



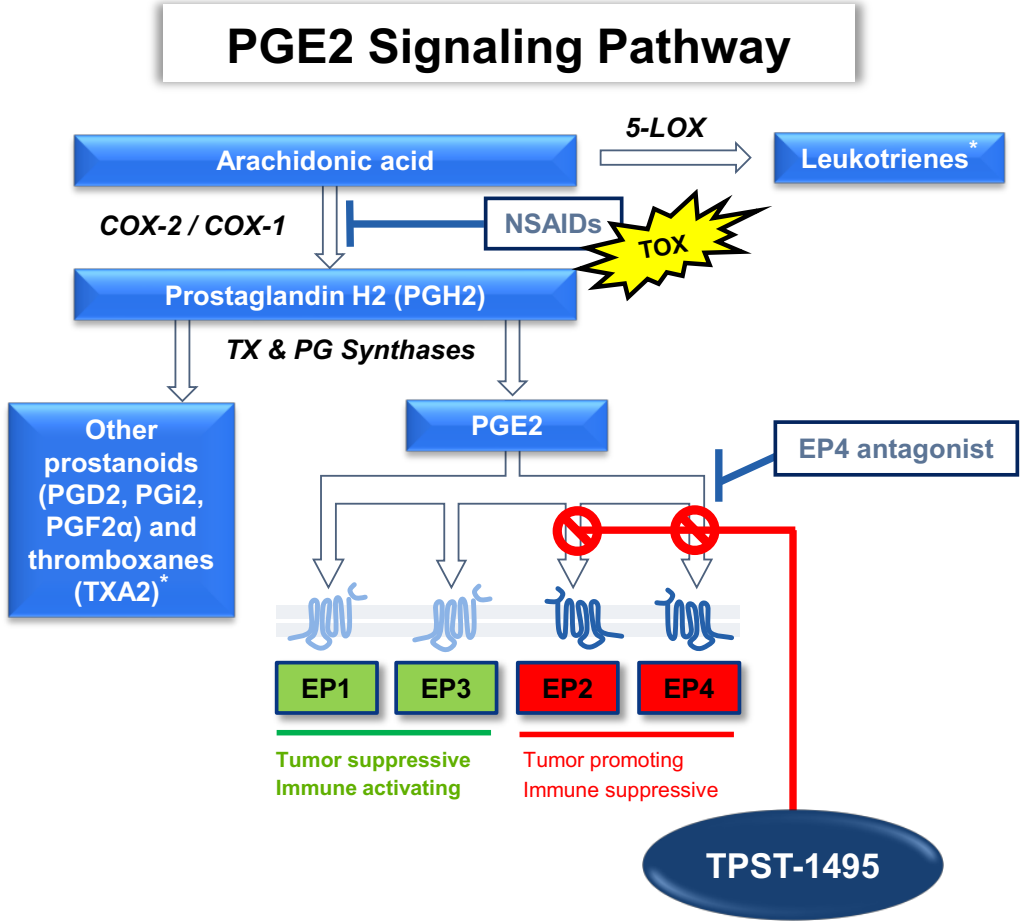
TPST-1495

First-in-Class Dual EP2/4 Antagonist – Moving to Phase 2 in FAP

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[1], 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

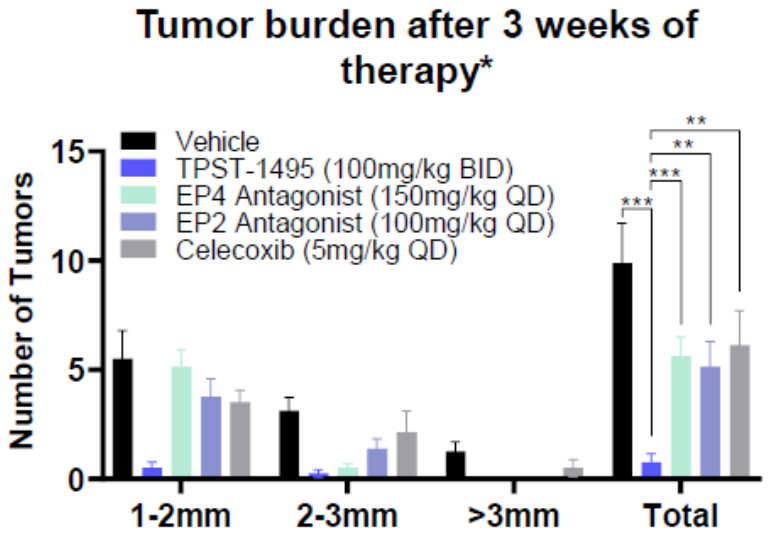


*Alterations in thromboxanes, prostacyclins and leukotrienes are associated with cardiovascular toxicity of NSAIDs

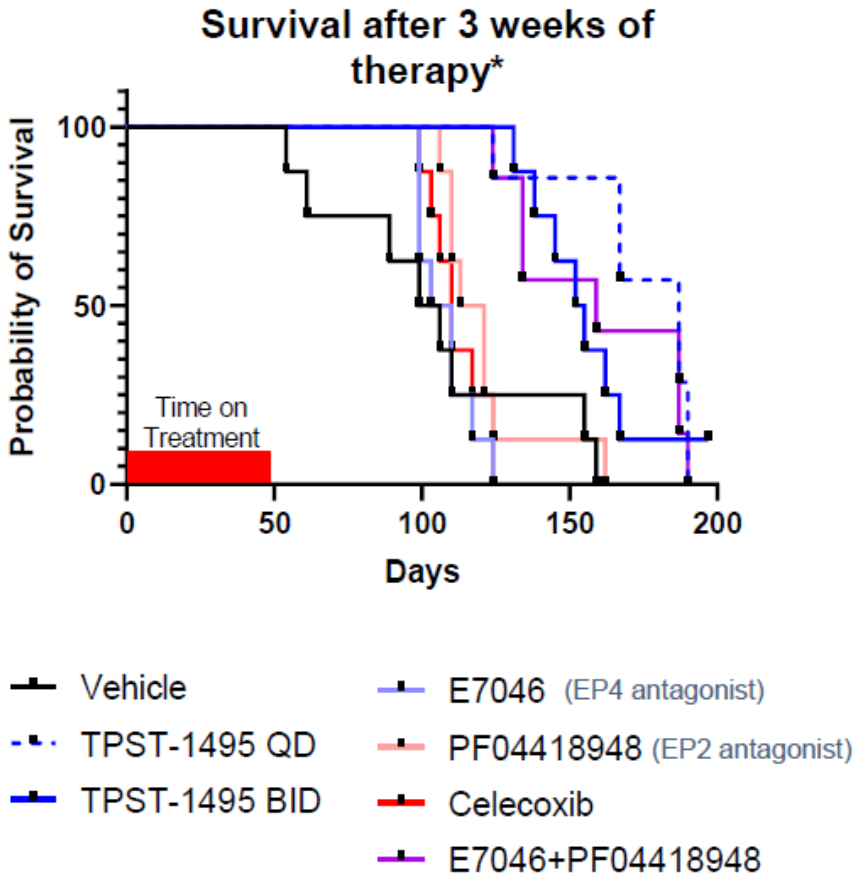
[1] If approved by FDA
[2] IC50s: 17 nM for EP2, 3 nM for EP4, and 51 nM in human whole blood assay

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

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



*Treatment initiated in 13-week-old mice.



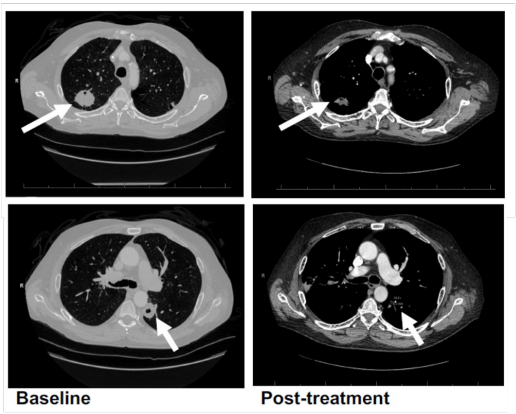
TPST-1495 Program Summary: Moving Forward in FAP

- **ASCO June 2023 Phase 1 Presentation**
  - 50 monotherapy, 24 in combination with pembrolizumab
  - Predominantly MSS CRC (61%) & heavily pre-treated (median 4 priors for monotherapy)

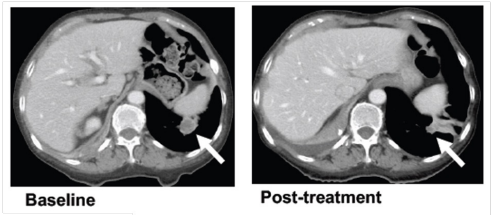
  Selected results highlighted in ASCO abstract:
  - Manageable toxicity mono and combo – no MTD but QD schedule more tolerable than BID schedule (=RP2 schedule)
  - DCR 43% (all SD) for monotherapy
    DCR 43% (including 1 PR in MSS CRC) for combination
  - PD activity observed in urine PGE2 metabolite and whole blood TNFα assay; endometrial patient with -22% tumor shrinkage had elevated COX-2 at baseline and increased CD8+ and GrB+TILs on treatment

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

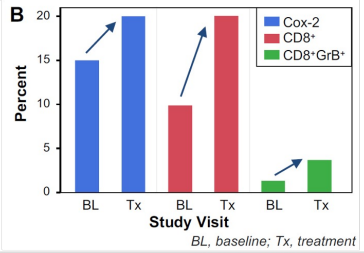
- ***4th line MSS-CRC*** *patient with confirmed RECIST Response (-38% BOR)*
- *Scans of lung met shrinkage were presented at ASCO*



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



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

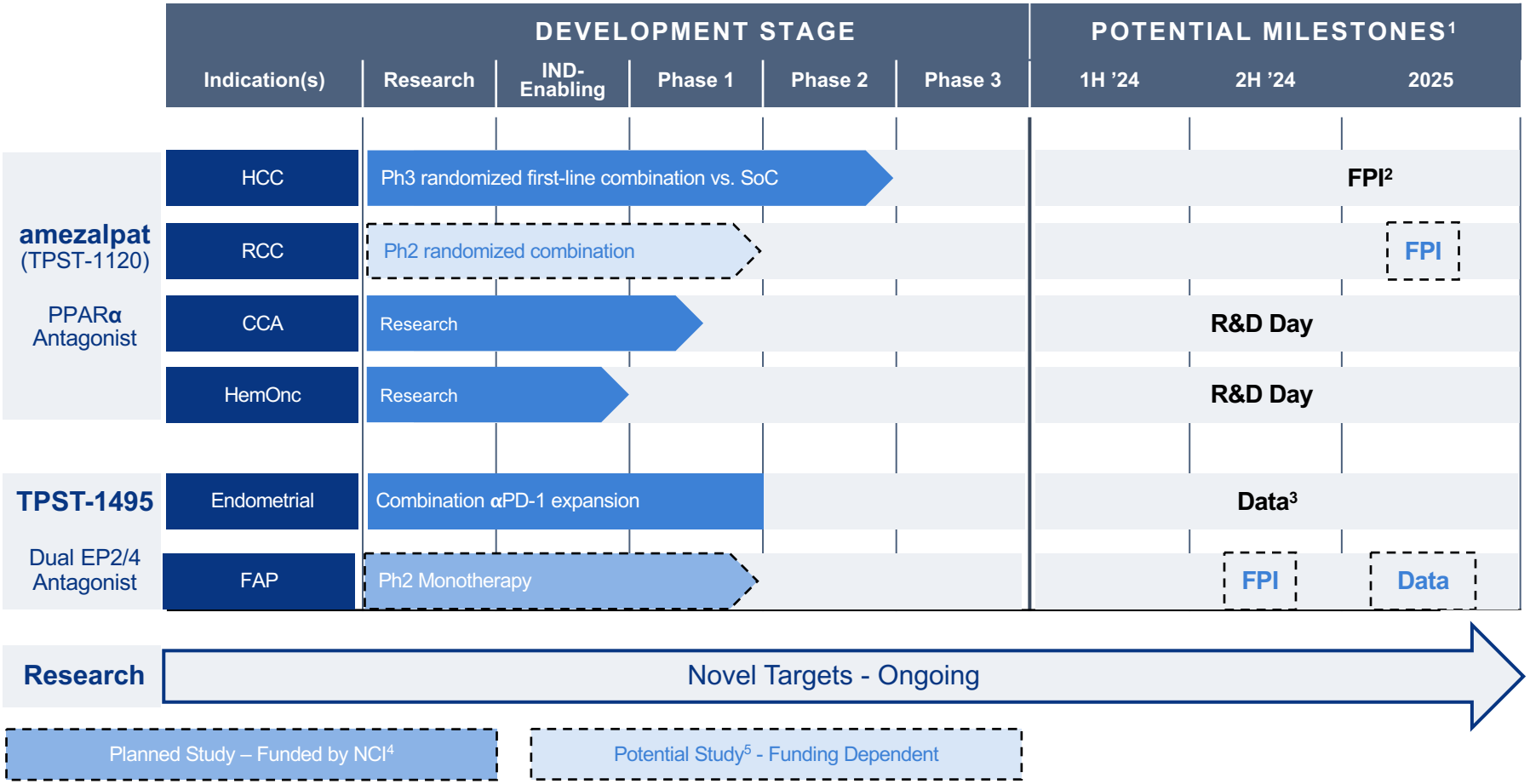


- **Familial Adenomatous Polyposis (FAP) Program**
  - No approved therapies for FAP (germline APC mutations)
  - Strong clinical support for PGE2 MOA (COX-2s effective, Accelerated Approval for celebrex)
  - Strong preclinical support for TPST-1495 based on $Apc^{Min/+}$ model
  - Working with FAP Consortium on an NCI-funded phase 2 study
  - Initial approval received from NCI; awaiting final approval
  - FPI in Phase 2 study expected in 2H24

Source: ASCO poster, data cut-off was 17-Apr-2023

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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[1] Timing is an estimate based on current projections and status of programs. [2] Projected for Q1 based on current estimates. [3] Either at a medical meeting (If accepted to present) or via another mechanism. [4] Initial approval by NCI received; awaiting final approval. [5] Interest based on existing data and MOA, but currently not funded.

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THERAPEUTICS

Company Overview

October 2024