



TEMPEST
THERAPEUTICS

Company Overview

January 2025

Forward-Looking Statements

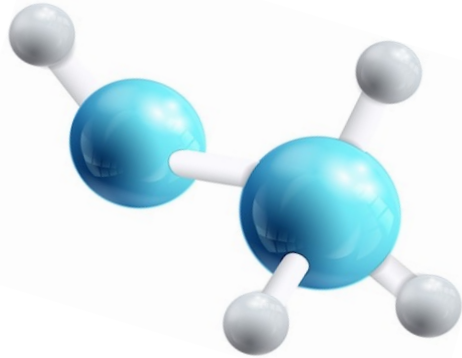
This presentation contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (the “Securities Act”) concerning Tempest Therapeutics, Inc. (“Tempest Therapeutics”). These 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 amezalpat¹ (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 September 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.

Amezalpat OS Data Complete Positive Data Set FDA & EMA Agreement on Phase 3 Plan



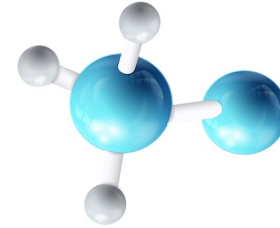
- ✓ **Amezalpat randomized 1L HCC data are superior to SoC arm**
 - OS data reveal six-month improvement with strong and stable hazard ratio
 - Biomarker data further support dual MOA of amezalpat
 - Large and growing commercial opportunity in HCC; positive data in RCC & CCA
- ✓ **Ownership and full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

Diversified Pipeline with Broad Potential - Spanning Discovery to Late-Stage



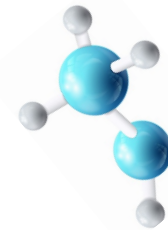
Amezalpat (TPST-1120) – Late Clinical

- PPAR α antagonist
- Strong positive randomized Ph2 data vs. SoC in first-line HCC – preparing for Ph3 start in Q1'25
- Additional positive data in RCC and CCA in ASCO Oral Presentation



TPST-1495 – Mid Clinical

- Dual EP2/4 antagonist
- Ph2 in FAP expected to start in Q1'25
- Ph1 data presented at ASCO



Discovery

Accomplished team exploring new solid tumor and hematologic malignancy programs

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

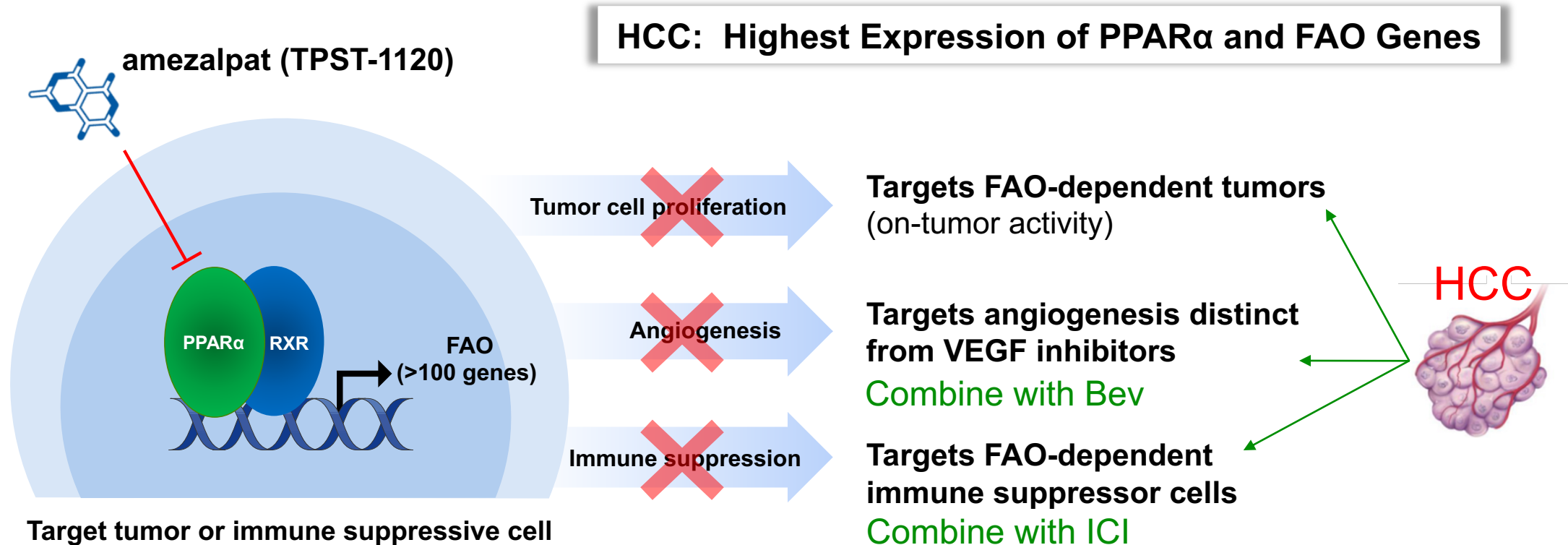
- ✓ OS hazard ratio 0.65 – positive at both topline and follow-up survival analyses
- ✓ Six-month improvement in median OS over control arm (21 months vs. 15 months)
- ✓ 20/40 patients remain in survival follow up in amezalpat arm vs. 9/30 in control
- ✓ Survival benefit maintained across key subpopulations, including PD-L1 negative
- ✓ Manageable safety profile similar to SOC
- ✓ FDA and EMA agreement on pivotal study
- ✓ Oral therapy with potential market advantages

Amezalpat (TPST-1120)

First-in-Class PPAR α Antagonist

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

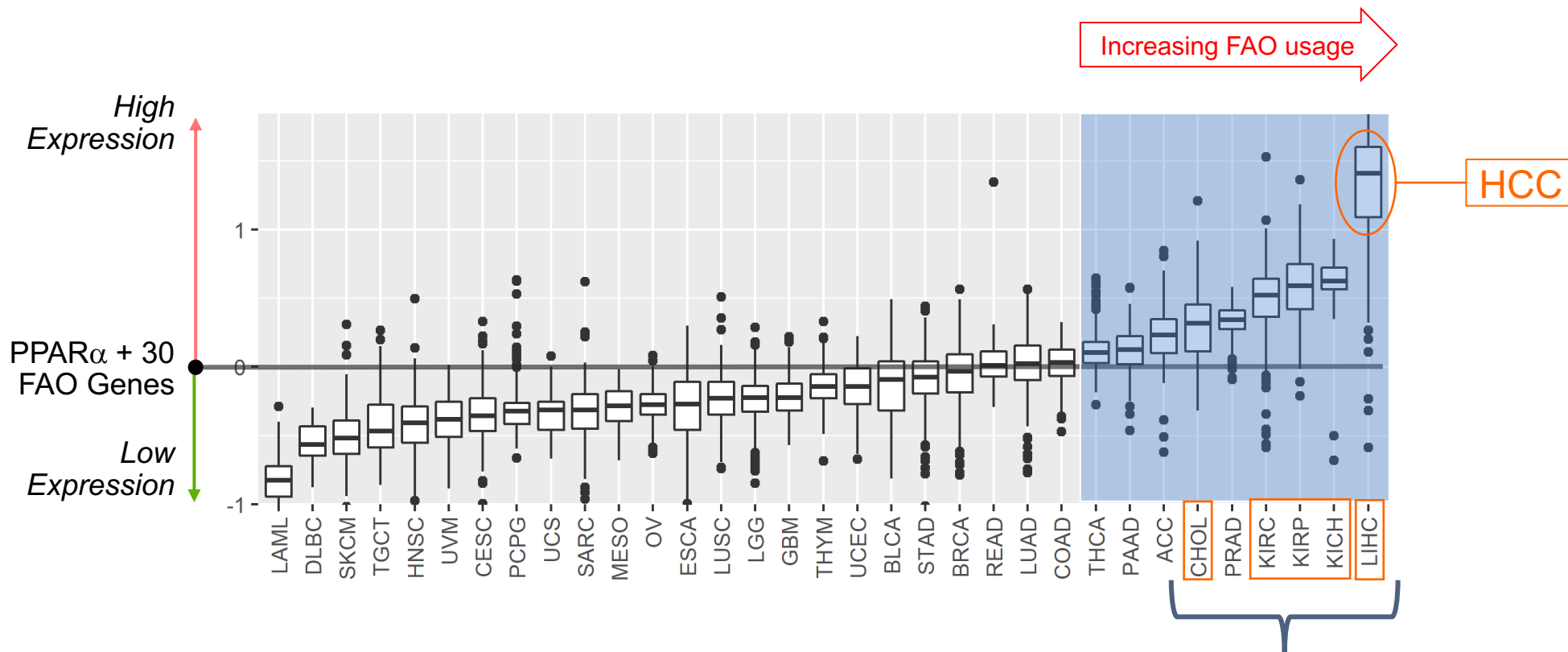
Phase 2 data support hypothesis that amezalpat will benefit HCC patients and improve activity of anti-VEGF & ICI therapy



PPAR α : Peroxisome Proliferator-Activated Receptor alpha

FAO-Dependent Tumors Inform Development Strategy

TCGA-based analysis of tumor metabolic gene expression profiles

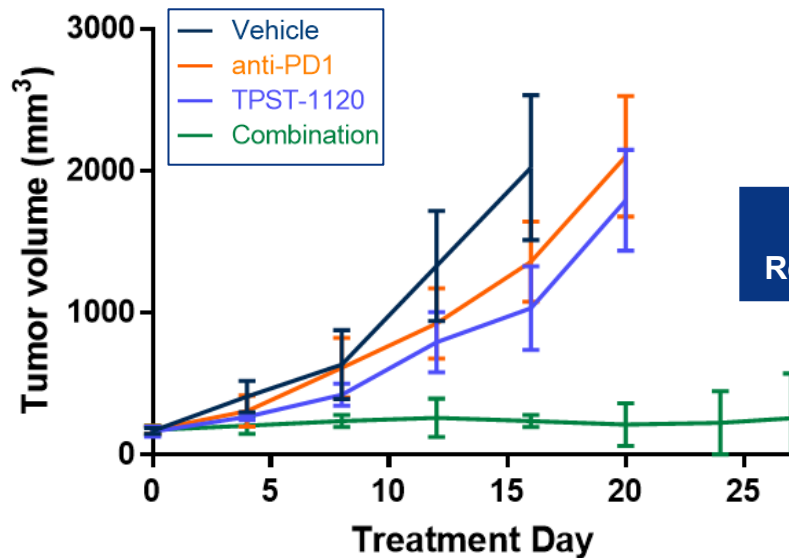


Positive patient data in HCC, RCC, and cholangiocarcinoma

Durable Responses in Combination with α -PD-1

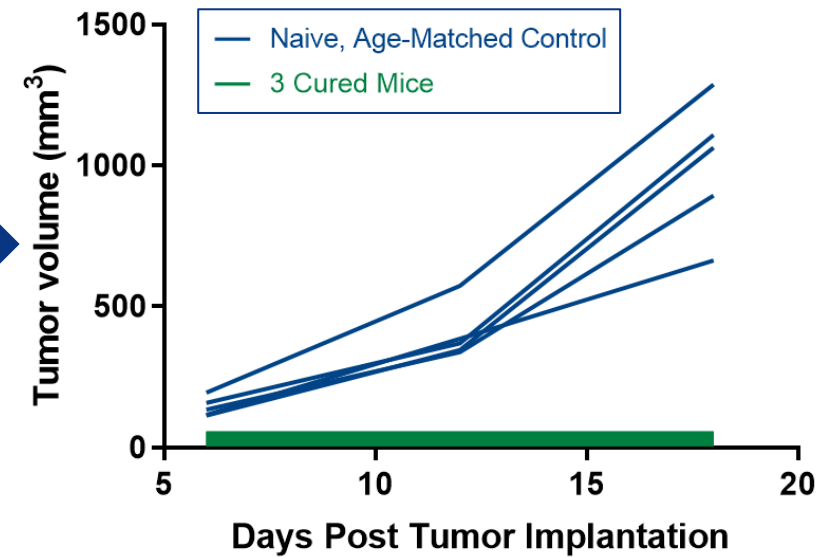
MC38 colorectal cancer tumor model, C57BL/6 immunocompetent mice

Amezalpat + anti-PD1 treatment



Tumor Re-challenge

Tumor re-challenge



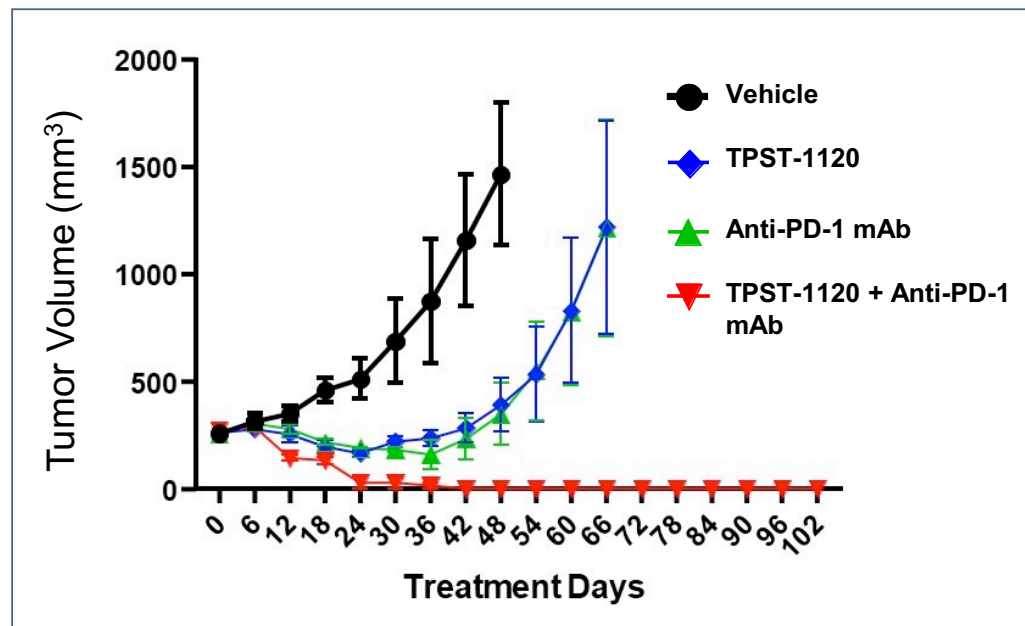
C57BL/6 mice bearing 150 mm³ MC38 flank tumors treated with TPST-1120 30 mg/kg BID and 200 μ g α -PD-1 Q3D

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}
- 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*



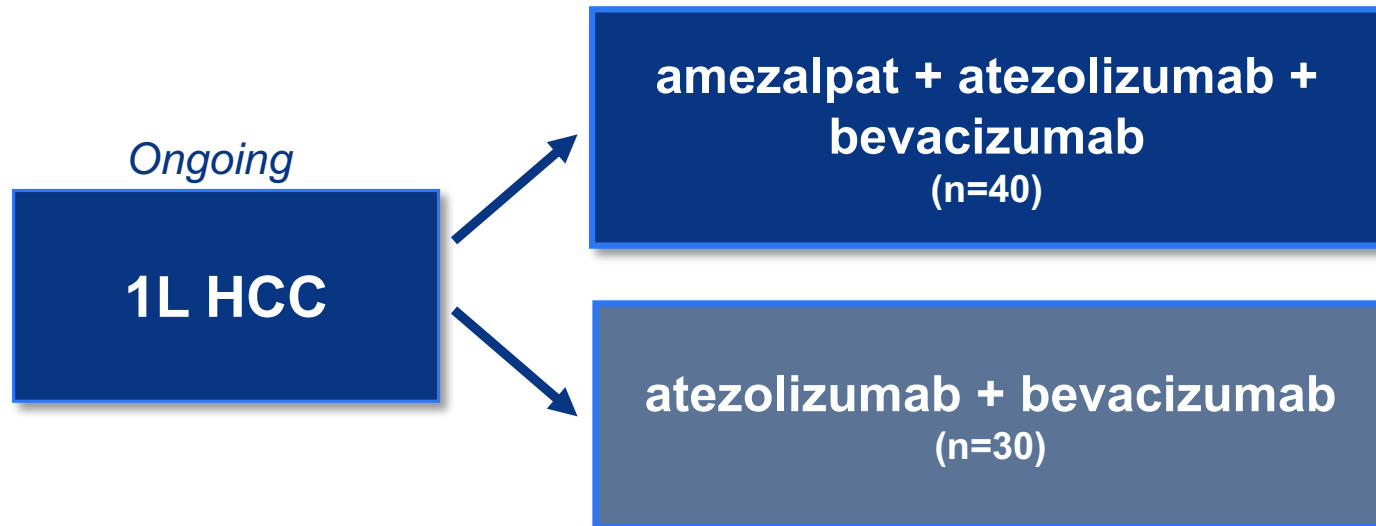
Amezalpat (TPST-1120) Randomized Phase 2 Data & Pivotal Plan

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 PPAR α and FAO Genes



- SoC 1L regimen +/- amezalpat
- 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

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)	Amezalpat + 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

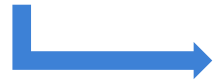
ECOG status, MVI/EHS, baseline NLR, PD-L1 status all favor the control arm, whereas AFP and region of enrollment favor the 1120 arm

^a ECOG status 0 indicates healthier patients ^b IMbrave150 update showed that atezo+bev regimen performed similarly in viral vs non-viral 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

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

Primary Global
Regulatory
Endpoint



	Atezo/Bev N=30	Amezalpat + 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)

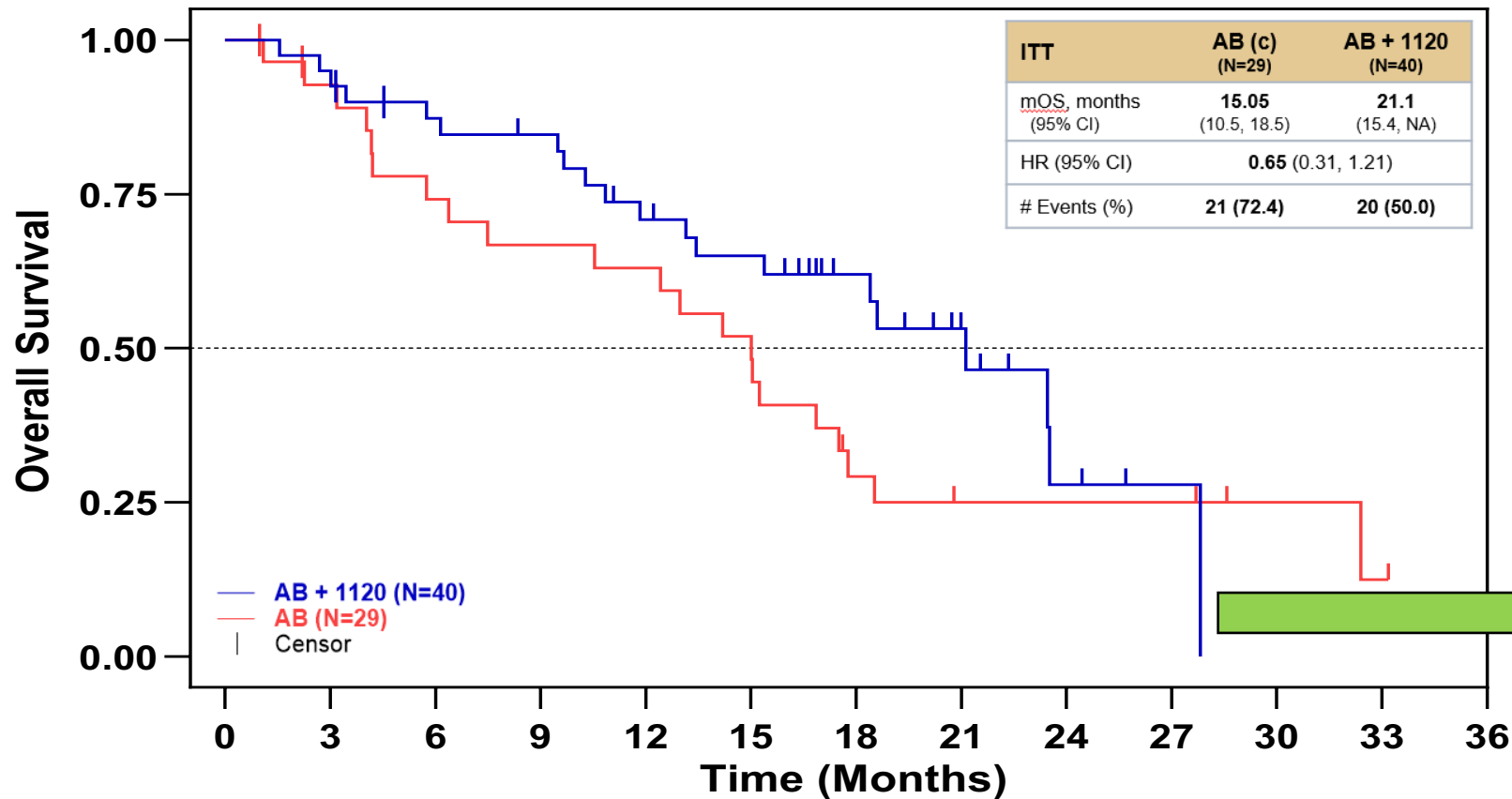


Consistent
Improvement
Across
All
Endpoints

- **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**

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-up¹



A Closer Look at HR

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

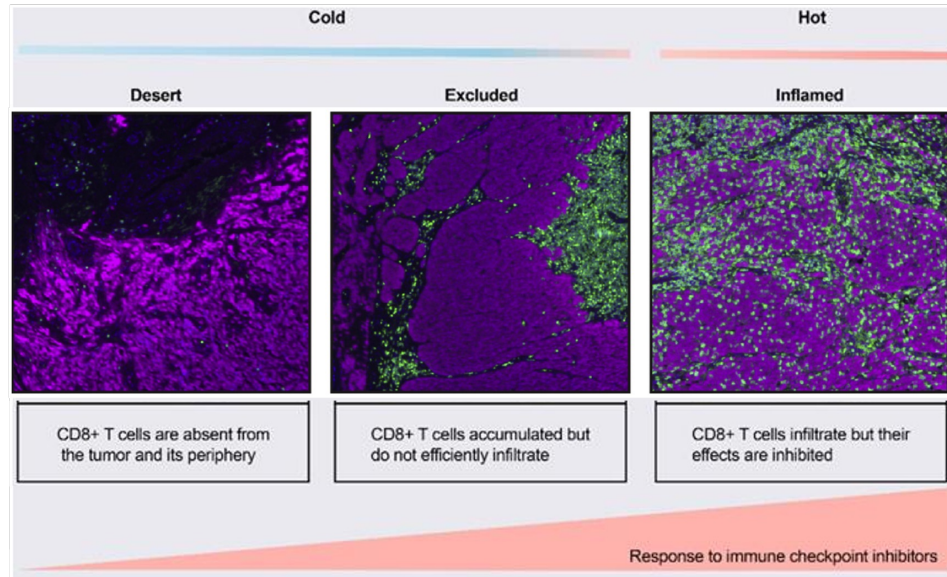
	Apr '23	Feb '24
HR	0.59	0.65
mOS	NR vs. 15	21 vs 15

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

	0	3	6	9	12	15	18	21	24	27	30	33	36
AB (control)	29	25	20	18	17	14	7	4	4	4	2	0	0
AB + 1120	40	38	33	31	25	22	14	8	3	1	0	0	0

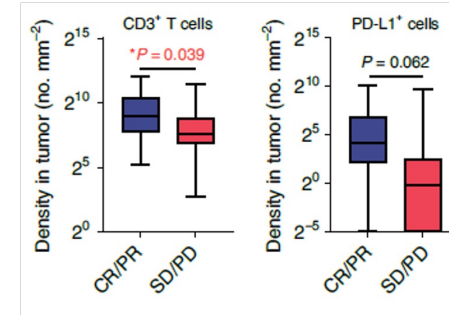
Amezalpat (TPST-1120) Improves ORR in Two Difficult Sub-populations

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

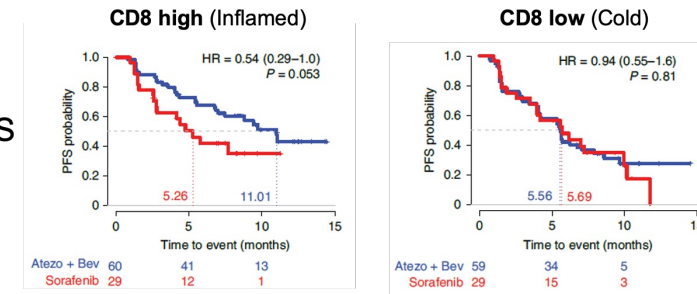


Tumor images representing 3 patterns of T cell infiltration visualized by CD3+ T cells (green) and a tumor marker (magenta). Van der Woude Trends in Cancer 2017.

ORR
Atezo/Bev



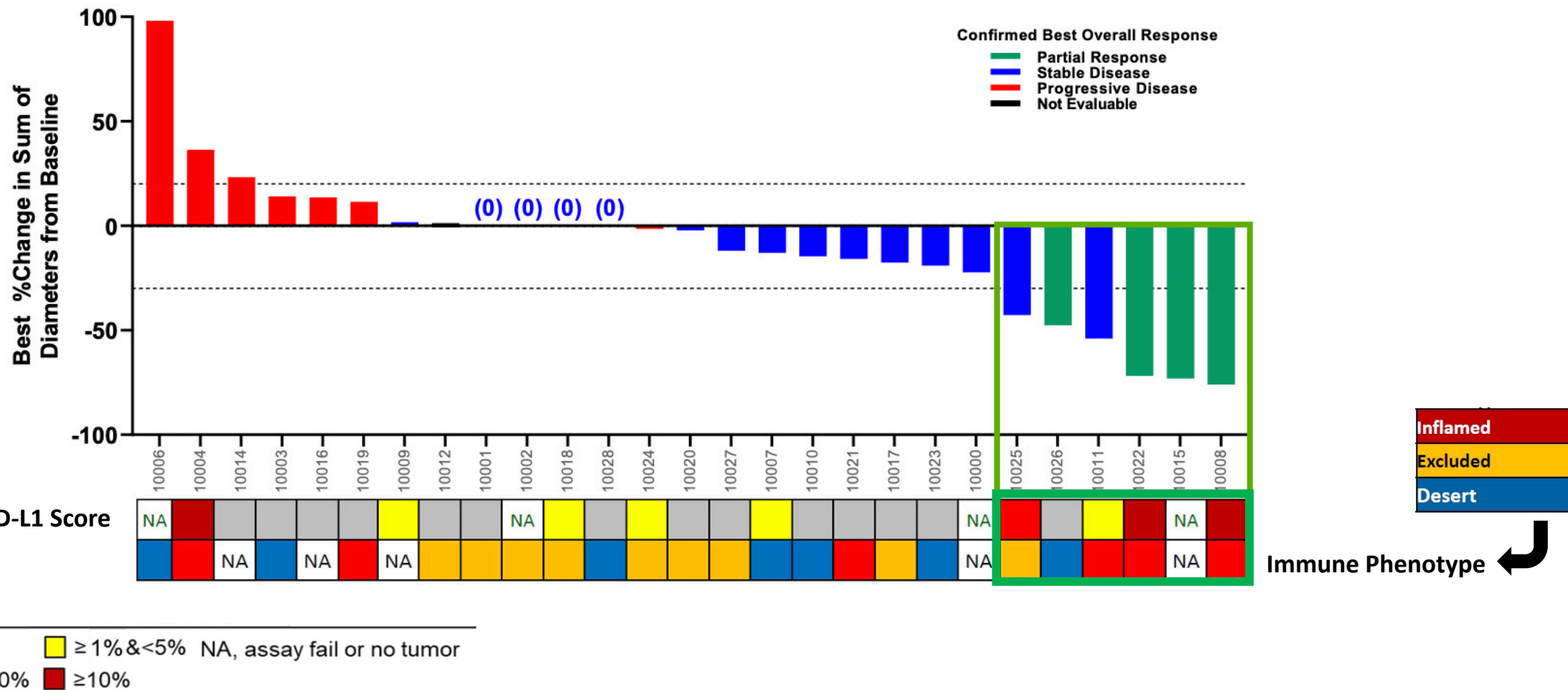
PFS



- 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 tumors⁶

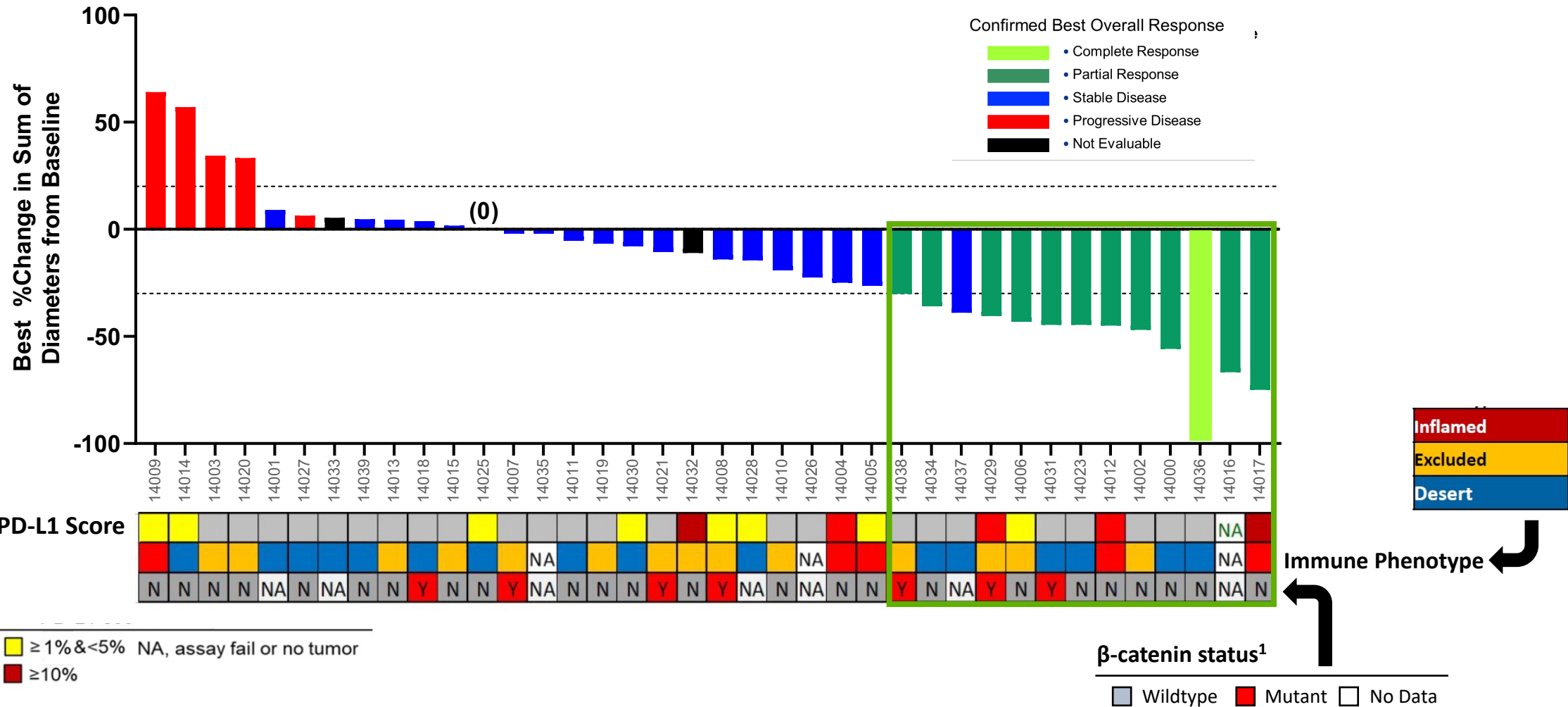
AB SoC Control Arm Responses Enriched for PD-L1+ and Hot Tumors

Atezo + Bev biomarker associations

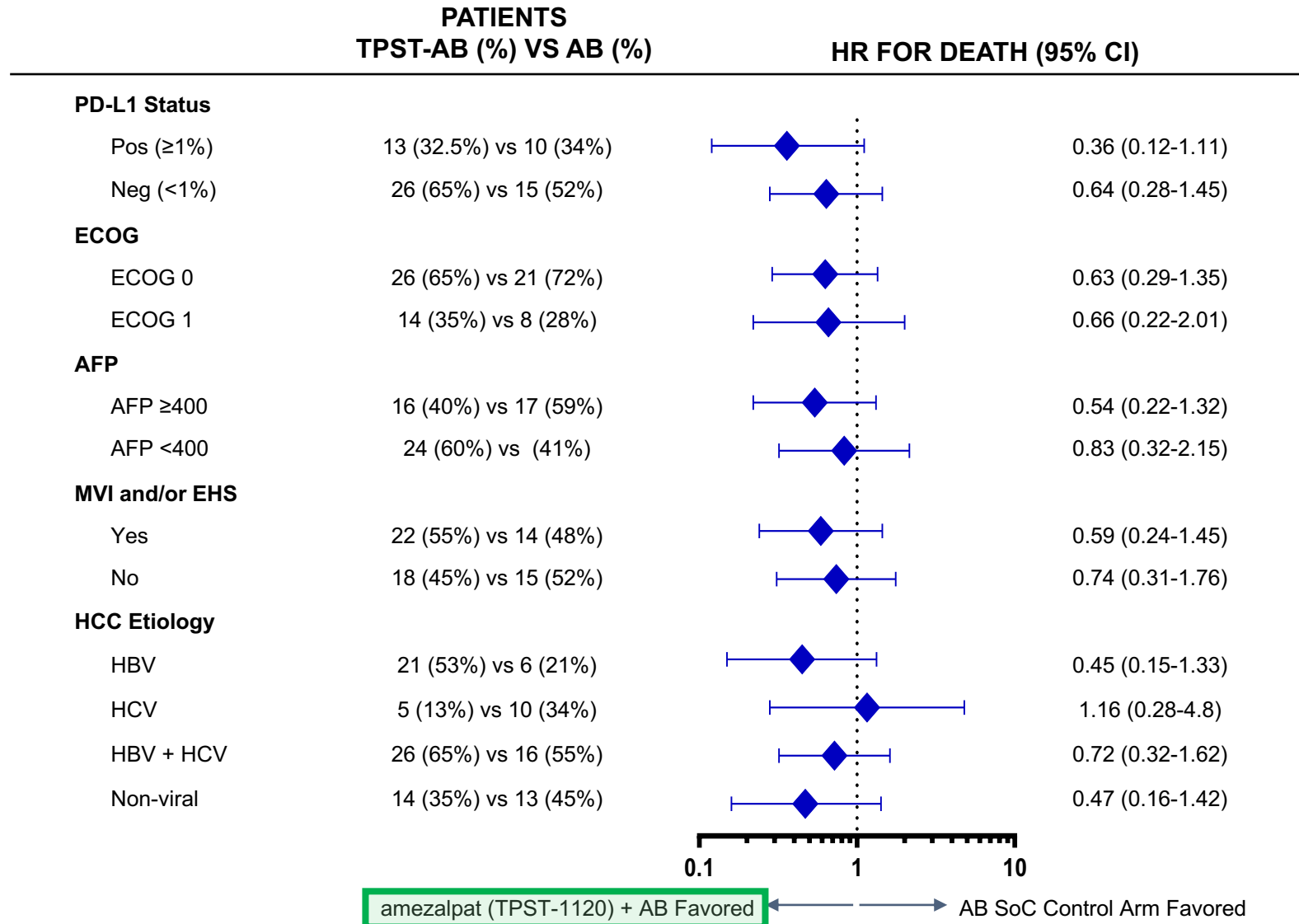


Amezalpat Responses Across the Board: Cold, Hot and β -catenin^{mut} & wt Tumors

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



Overall Survival Benefit Maintained Across Key Subpopulations



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)	Amezalpat + 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

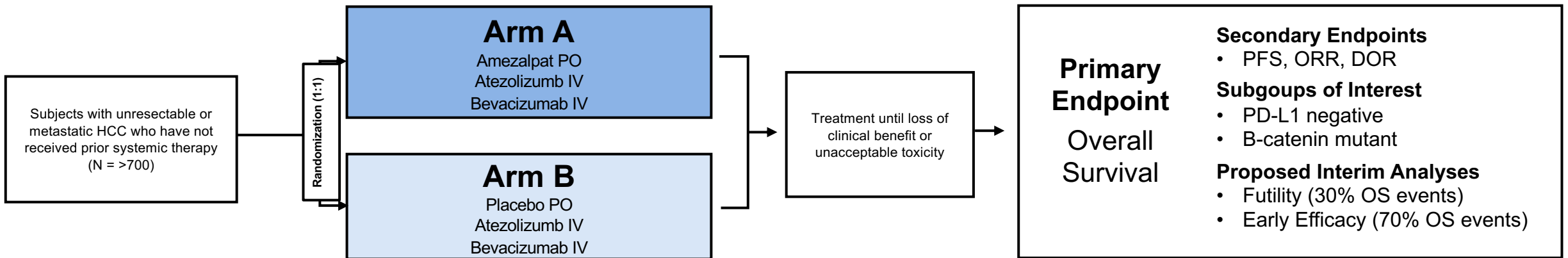
Data as of Feb 14, 2024

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

Data as of April 20, 2023

Pivotal Phase 3 Study Design – FDA and EMA Agreement

- 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:

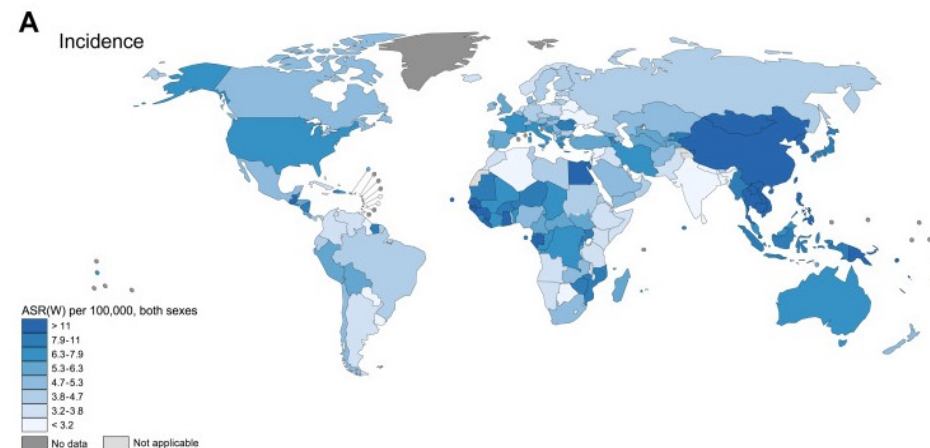
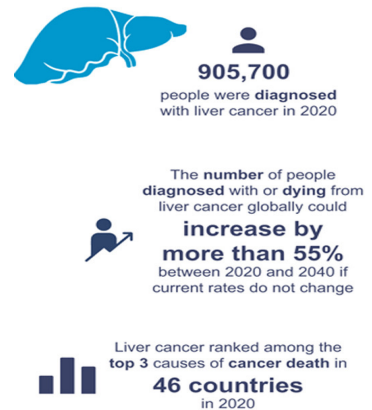
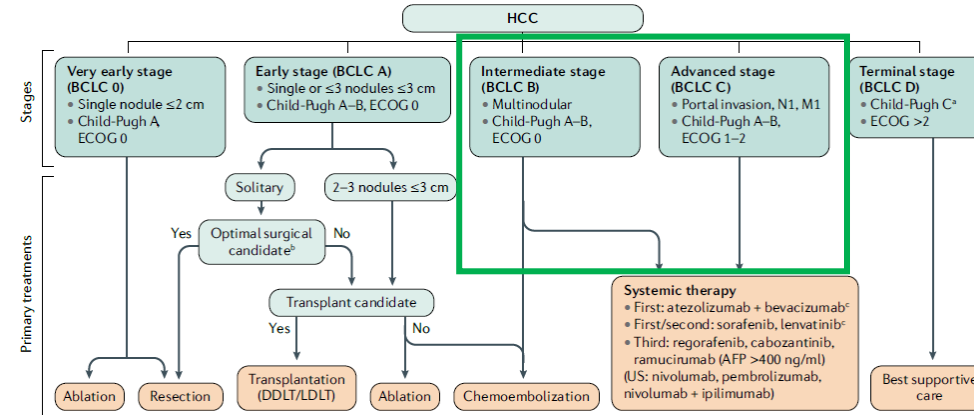
- 90% power
- 2-sided 5% alpha
- Critical hazard ratio² of <.805 for primary efficacy and <.729 for early efficacy (compare to .65 in Phase 2)
- Control arm assumption based on longer historical value, as opposed to shorter Phase 2 & RW data
- 1:1, >700 subjects

First-Line HCC is a Large, Growing and Uncrowded Market

Amezalpat'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



¹ To the company's knowledge, amezalpat is the latest stage and only PPAR α antagonist in clinical development

Runggay, 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%20is%20Pharma%20Day%20on%2011th%20September%202023%20in%20London>. Accessed Jan 2024.

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

- ✓ OS hazard ratio 0.65 – positive at both topline and follow-up survival analyses
- ✓ 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 and EMA agreement on pivotal study
- ✓ Oral therapy with potential market advantages

Amezalpat Phase 1 Data

Supports Expanded Oncology Franchise (RCC, CCA)

ASCO 2022 - Oral Presentation

Anti-Tumor Activity Observed in Amezalpat (TPST-1120) Phase 1 Study

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

Monotherapy

3+3 Design
Amezalpat up to 600 mg BID

Combo with α PD-1 (nivo)

3+3 Design
Amezalpat 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

Amezalpat Has A Manageable Safety Profile Consistent with Phase 2 Data

Treatment-related adverse events occurring in ≥ 2 Patients

AE, n (%)	Amezalpat 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 (%)	Amezalpat + 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

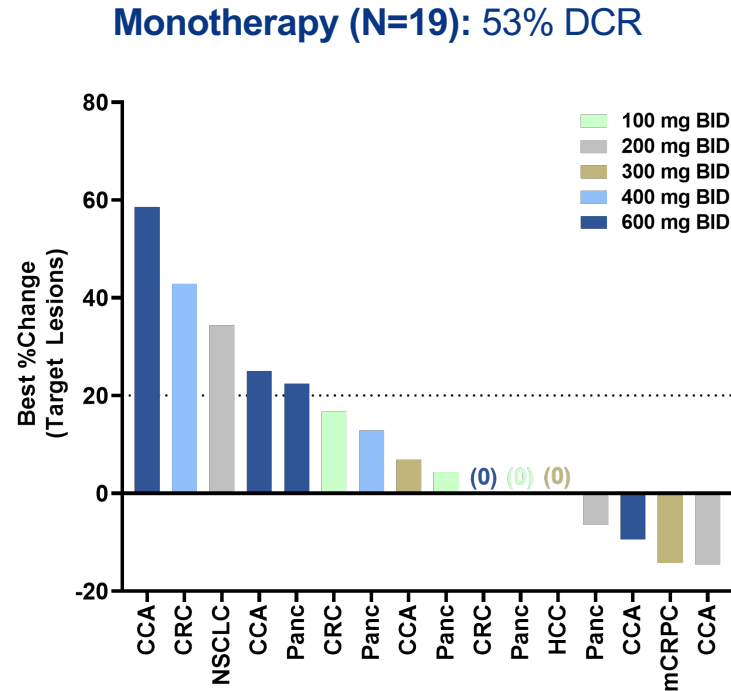
[^]Arthralgia, Hepatic enzymes increased, Muscle spasms

*Related to either TPST-1120 or nivolumab

- Amezalpat 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

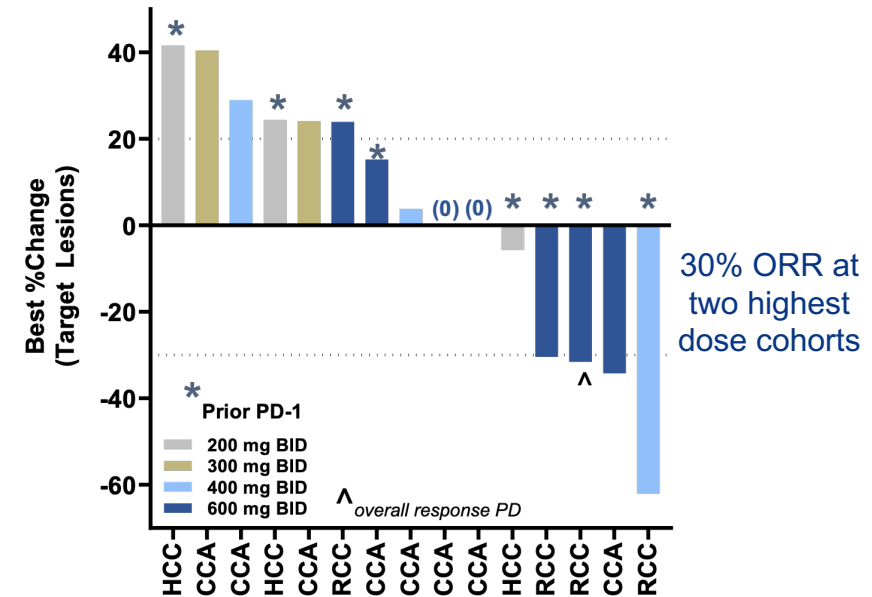
Phase 1 Amezalpat Activity Across Multiple Tumor Types

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



- 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



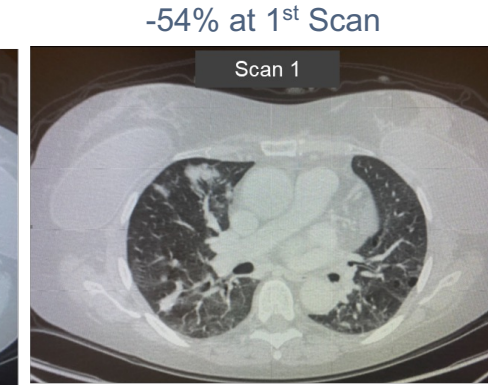
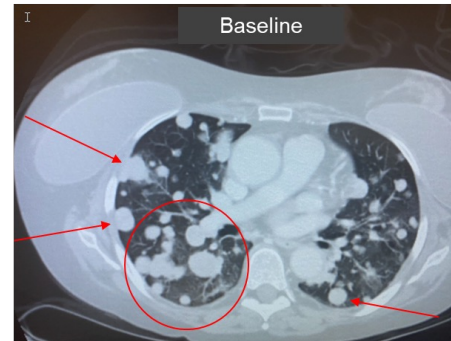
- Responses in patients with IO refractory (RCC) or IO non-responsive (CCA) indications
- All patients received approved α -PD1
- Responses in two highest dose cohorts

RCC Responses with Amezalpat + 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



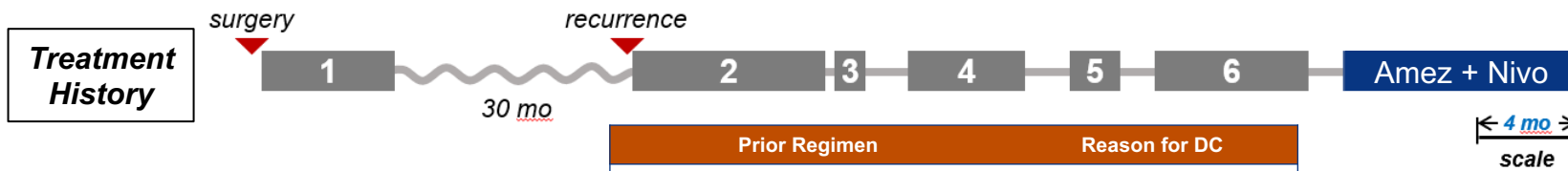
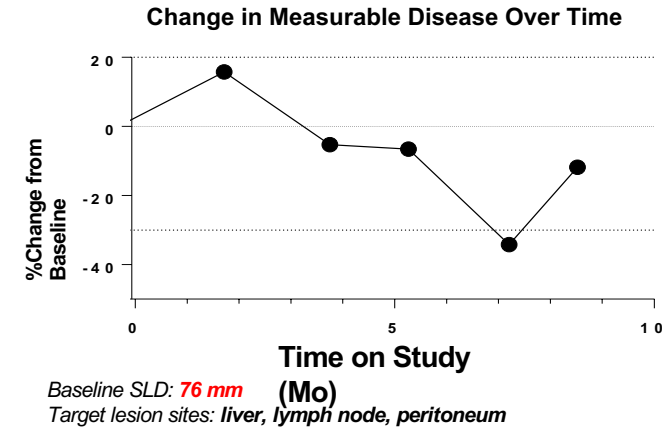
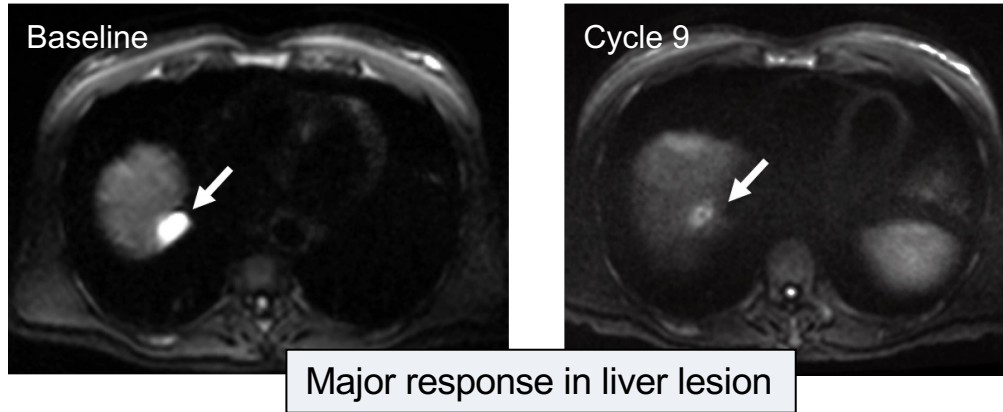
Subject 22-008

- 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 amezalpat reverses T cell exhaustion

Cholangiocarcinoma Response with Amezalpat + Nivolumab

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



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

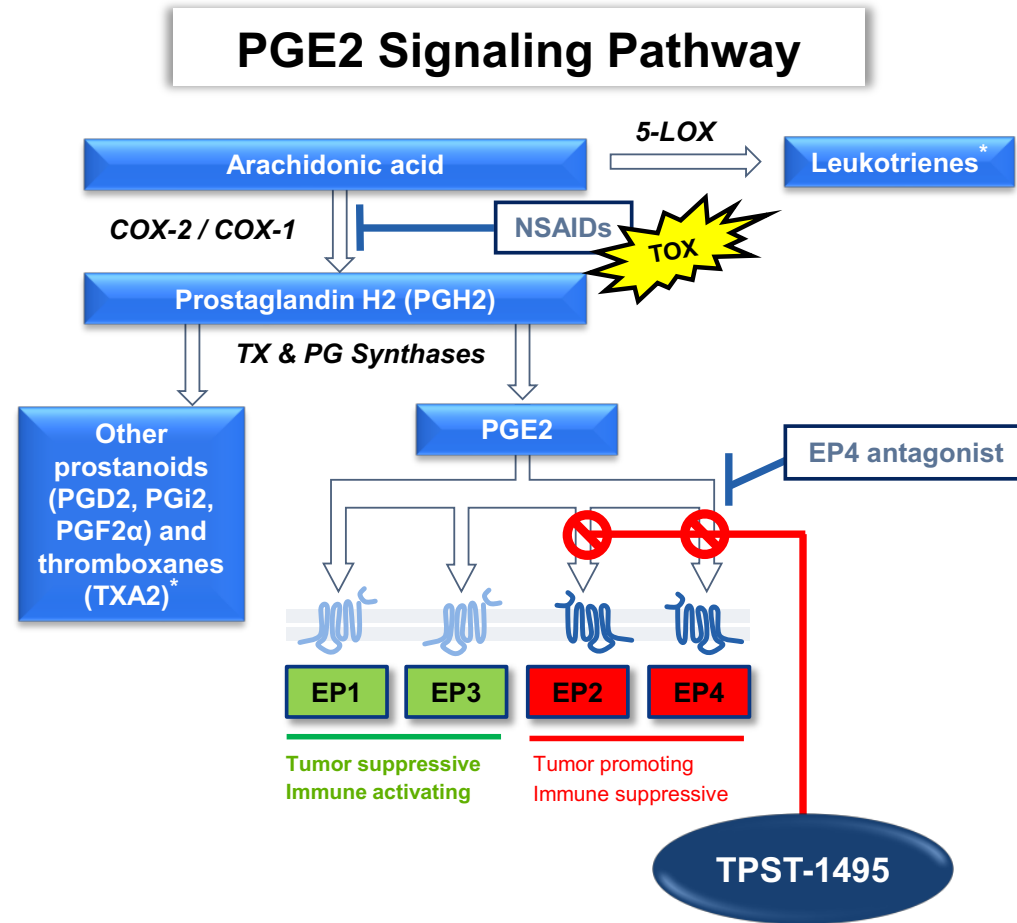
TPST-1495

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

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 class¹, highly specific antagonist inhibits *only* the tumor promoting EP2 and EP4 receptors
 - Oral therapy
 - Nanomolar potency²
 - Targets *both* tumor cells and immune suppressive cells

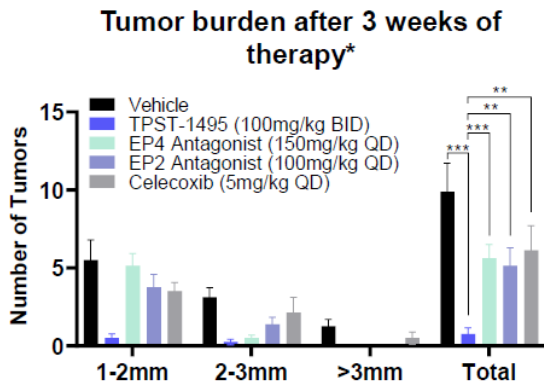


*Alterations in thromboxanes, prostacyclins and leukotrienes are associated with cardiovascular toxicity of NSAIDs

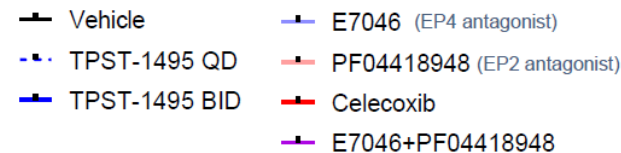
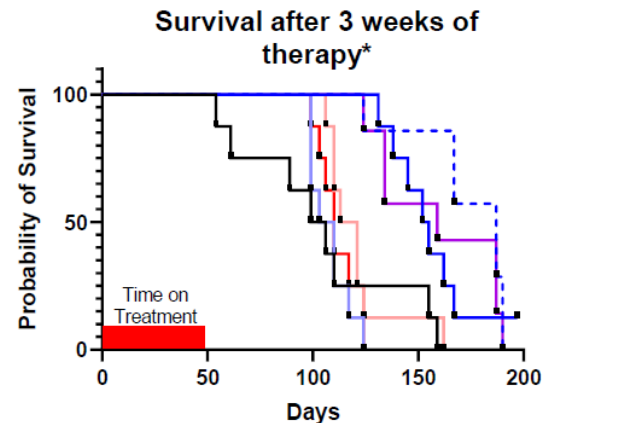
TPST-1495 Program Summary: Moving Forward in FAP Phase 2

TPST-1495 therapy conferred a significant survival advantage compared to other prostaglandin pathway inhibitors

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



*Treatment initiated in 13-week-old mice.



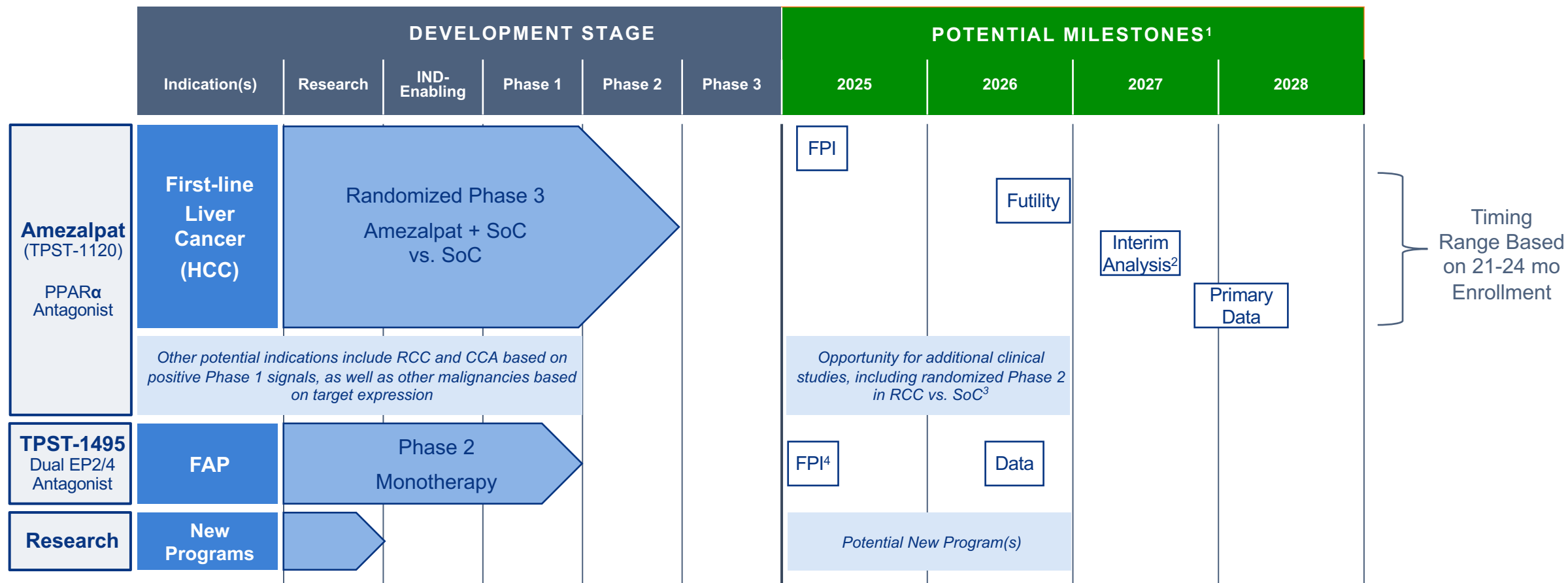
Familial Adenomatous Polyposis (FAP) Program

- 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
- To be funded by NCI
- FPI in Phase 2 study expected in 1H25, data in 2026



Evolution to Pivotal Development in Large 1L HCC Indication

Amezalpat (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; "FPI" First Patient In



TEMPEST
THERAPEUTICS

Company Overview

January 2025