

# Amezalpat (TPST-1120) Randomized 1L HCC Data Update

June 20, 2024 – Conference Call

#### **Forward-Looking Statements**

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### Amezalpat (TPST-1120): First-in-Class<sup>1</sup> PPARα Antagonist

Targets both tumor cells and immune suppressive cells



**PPARα:** Peroxisome Proliferator-Activated Receptor alpha



<sup>1</sup>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

IPEST Source: <u>https://www.cancer.gov/ccg/research/genome-sequencing/tcga</u>

"TCGA" = The Cancer Genome Atlas Program, "HCC" = hepatocellular carcinoma, "RCC" = renal cell carcinoma, "NSCLC" = non-small cell lung cancer, "CRC" = colorectal cancer

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

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





<sup>1</sup> Morpheus HCC study in collaboration with Roche (NCT04524871); IE criteria based on pivotal IMbrave 150

# Superior OS to SoC and Manageable Safety Profile Going Into Phase 3

Amezalpat triplet is superior in the main regulatory endpoint (OS); safety profile may confer additional commercial benefit



0.65 hazard ratio for OS – stable since primary analysis 10 months earlier (0.59)

Early and persistent separation of survival curves

 $\checkmark$ 

Six-month improvement in median OS over control arm (21 months vs. 15 months)



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



Survival benefit maintained across key subpopulations



Manageable safety profile consistent with MOA and Phase 1 data



Late conversion of PR to CR in immune cold, PD-L1 negative, b-catenin wild-type tumor



### **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	Oª	22 (73.3%)	26 (65.0%)
Disease due to viral hepatitis <sup>b</sup>	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 <sup>c</sup>	≥5	4 (13.3%)	11 (27.5%)
PD-L1 Negative	Neg (TAP<1)	15 (60%) <sup>d</sup>	26 (67%) <sup>e</sup>

ECOG status, MVI/EHS, baseline NLR, PD-L1 status all favor the control arm, whereas AFP and region of enrollment favor the 1120 arm <sup>a</sup> ECOG status 0 indicates healthier patients <sup>b</sup> IMbrave150 update showed that atezo+bev regimen performed similarly in viral vs non-viral disease<sup>1</sup> <sup>c</sup> A number of recent studies have reported that baseline NLR is predictive of ORR and/or OS in HCC with atezo + bev regimen<sup>2</sup>. <sup>d</sup>25 subjects PD-L1 evaluable; <sup>e</sup>39 subjects PD-L1 evaluable



<sup>1</sup> 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. <sup>2</sup> 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)	<b>7m</b> (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 <sup>1</sup>	43% (100% DCR)

- Biomarkers and pharmacodynamic data support MOA of TPST-1120
  - 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-up<sup>1</sup>





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

#### Atezo + Bev biomarker associations



≥1%&<5% NA, assay fail or no tumor</p>

≥%5&<10% ≥10%



### Amezalpat Responses Across the Board: Cold, Hot and β-catenin<sup>mut & wt</sup> Tumors





#### **Overall Survival Benefit Maintained Across Key Subpopulations**

	PATIENTS TPST-AB (%) VS AB (%)	HR FOR DEATH (95% CI)
PD-L1 Status		
Pos (≥1%)	13 (32.5%) vs 10 (34%) ⊢	0.36 (0.12-1.11)
Neg (<1%)	26 (65%) vs 15 (52%)	0.64 (0.28-1.45)
ECOG		
ECOG 0	26 (65%) vs 21 (72%)	0.63 (0.29-1.35)
ECOG 1	14 (35%) vs 8 (28%)	0.66 (0.22-2.01)
AFP		
AFP ≥400	16 (40%) vs 17 (59%)	0.54 (0.22-1.32)
AFP <400	24 (60%) vs (41%)	0.83 (0.32-2.15)
MVI and/or EHS		
Yes	22 (55%) vs 14 (48%)	0.59 (0.24-1.45)
No	18 (45%) vs 15 (52%)	0.74 (0.31-1.76)
HCC Etiology		
HBV	21 (53%) vs 6 (21%)	0.45 (0.15-1.33)
HCV	5 (13%) vs 10 (34%)	1.16 (0.28-4.8)
HBV + HCV	26 (65%) vs 16 (55%)	0.72 (0.32-1.62)
Non-viral	14 (35%) vs 13 (45%)	0.47 (0.16-1.42)



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







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

<sup>†</sup>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



### Preliminary Pivotal Phase 3 Study Design

Appropriately sized with proposed planned analyses could shorten timeline<sup>1</sup>



Stratification factors:<sup>2</sup>

- 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
- Control arm assumption based on historical value
- 1:1, >700 subjects



### First-Line HCC is a Large and Uncrowded Market

#### TPST-1120's MoA and lead position offers a unique opportunity<sup>1</sup> 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







<sup>1</sup> To the company's knowledge, TPST-1120 is the latest stage and only PPAR $\alpha$  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.



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