Tempest Announces Positive Early Results from Global Randomized Phase 1b/2 Combination Study of TPST-1120 in First-Line Hepatocellular Carcinoma

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- *Positive randomized data with TPST-1120 combined with atezolizumab + bevacizumab compared head-to-head with atezolizumab + bevacizumab*
- *The addition of TPST-1120 resulted in a clinically-meaningful improvement in both confirmed and unconfirmed RECIST responses*
- *The number of patients on treatment and on study markedly favors the TPST-1120 arm*
- *Company to host webcast conference call today at 8:30 a.m. ET*

BRISBANE, Calif., April 28, 2023 (GLOBE NEWSWIRE) -- Tempest Therapeutics, Inc. (Nasdaq: TPST), a clinical-stage oncology company developing first-in-class[1] therapeutics that combine both targeted and immune-mediated mechanisms, today announced positive early results from a global randomized Phase 1b/2 clinical study in which TPST-1120, Tempest's small molecule PPAR α antagonist, demonstrated clinically-meaningful improvement in multiple categories when combined with the standard-of-care regimen of atezolizumab and bevacizumab in a randomized comparison to atezolizumab and bevacizumab in the first-line treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC).

Data from 40 patients in the TPST-1120 arm randomized per protocol against 29 evaluable (30 total) patients in the control arm showed:

- **Unconfirmed responses** of 30% for the TPST-1120 triplet arm (12/40) vs. 17.2% for the control arm (5/29), demonstrating a **74.4% relative improvement in objective response rate (ORR);**
- **Confirmed responses** of 17.5% for the TPST-1120 triplet arm (7/40) vs. 10.3% for the control arm (3/29), demonstrating a **69.9% relative improvement in confirmed ORR;**
- **47.5%** (19/40) of the TPST-1120 arm patients are **on treatment vs. 23.3%** (7/30) in the control arm;
- **80%** (32/40) of the TPST-1120 arm patients are **on study vs. 50%** (15/30) in the control arm;
- The addition of TPST-1120 was **well tolerated**, with safety data consistent with the control regimen; and,
- The **randomized arms were generally well balanced** at baseline for prognostic factors.

In the IMbrave150 Phase 3 trial, confirmed ORR benefit correlated with overall survival (OS) benefit.[2]

The study was conducted in clinical collaboration with F. Hoffman La-Roche. Secondary endpoints include duration of response (DoR), progression free survival (PFS) and OS, which are immature as of the data cut and will be potentially available later in the year or next year. Enrollment began in fall of 2021 and the cutoff date for these data was February 8, 2023, which was greater than six weeks after the last patient enrolled and allows for all patients to have had at least one scan. Tempest expects the full data set to be presented by Roche at a medical meeting at a later date. ORR was determined by RECIST v1.1, and confirmed responses included at least two scans.

"These randomized data in first-line HCC are exciting and support the promise of TPST-1120 as an active small molecule for patients," said Stephen Brady, chief executive officer of Tempest. "HCC is a common and aggressive cancer where significant unmet need remains to improve care in the first line and beyond. We believe the improvements shown in the TSPT-1120 arm validate the hypothesis of targeting HCC with TPST-1120, as well as the mechanistic basis for combination with both a checkpoint inhibitor and VEGF inhibitor. We look forward to receiving more data this year, including with respect to potential biomarkers, and to the potential next steps of this program in HCC and other cancers of interest."

"HCC is one of the few tumor types with increasing mortality in the United States," said Mark Yarchoan, M.D., Associate Professor of Medical Oncology at Johns Hopkins School of Medicine. "Atezolizumab + bevacizumab is the current preferred frontline therapy, and the addition of TPST-1120 appears to be active and well tolerated. Response rates in HCC can vary significantly across studies, and therefore the use of a randomized, controlled study design instead of a historical control is a strength of this study. The numerically higher response rate and proportion of patients on study with the addition of TPST-1120 is promising. I believe that this is an active agent and I look forward to further clinical development of TPST-1120."

Conference Call & Webcast Information

Tempest will host a webcast conference call today, April 28, 2023 at 8:30 a.m. ET.

To join the conference call via phone and participate in the live Q&A session, please pre-register online here to receive a telephone number and unique passcode required to enter the call. The live webcast and audio archive of the presentation may be accessed on the investor section of the Tempest website at https://ir.tempesttx.com/. The webcast will be available for replay for 30 days.

About the Randomized Clinical Trial

The Phase 1b/2 global randomized HCC study is part of Roche's Morpheus program and evaluates TPST-1120 in combination with the standard-of-care regimen of atezolizumab and bevacizumab in patients with unresectable or metastatic HCC not previously treated with systemic therapy. To date, the trial has enrolled 70 patients to the 1120 arm and contemporaneous control arm at ~25 sites worldwide including in the United States and Europe, who received either the TPST-1120 combination or the standard-of-care regimen of atezolizumab and bevacizumab with primary efficacy endpoint of objective response rate, and key secondary endpoints including PFS and OS. Under the terms of the clinical collaboration agreement, Roche managed the study operations for this global, multicenter trial.

About TPST-1120

TPST-1120 is an oral, small molecule, selective PPARα antagonist wholly-owned by Tempest. Tempest's preclinical data suggest that TPST-1120 can kill tumor cells directly and target suppressive immune pathways in the tumor microenvironment. Both types of targeted cells can be dependent on fatty acid metabolism, which is regulated by the PPARα transcription factor. In extensive non-clinical studies, TPST-1120 as a monotherapy or in combination with other anti-cancer drugs resulted in significant reductions in tumor growth and stimulation of durable anti-tumor immunity. In a Phase 1 clinical trial in patients with heavily-pretreated advanced solid tumors, TPST-1120 as monotherapy and in combination with the PD-1 inhibitor nivolumab demonstrated tumor reduction (including according to RECIST criteria), as well as biomarker modulation. TPST-1120 was well-tolerated both as a monotherapy and in combination with nivolumab.

About Hepatocellular Carcinoma

HCC is an aggressive cancer with rising mortality and is projected to become the third leading cause of cancer death by 2030.[3] Every year, more than 900,000 people worldwide are diagnosed with HCC.[4] Incidence and mortality are highest in East Asia and are increasing in parts of Europe and the US.[5] In the US, HCC represents the fastest-rising cause of cancer-related death.[3]

Nine out of ten cases of HCC are caused by chronic liver disease, which includes chronic hepatitis B and C infection, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), alcohol-related liver disease (ALD) and cirrhosis resulting from these conditions.[6]

Even if diagnosed in the early stage, an estimated 70-80% of people with early-stage HCC experience disease recurrence following surgery.[7] Early recurrence is associated with poorer prognosis and shorter survival.[5,8] Tumor size, number of tumors, and portal vein invasion are associated with an increased risk of recurrence.[6]

About Tempest Therapeutics

Tempest Therapeutics is a clinical-stage oncology company advancing small molecules that combine both tumor-targeted and immune-mediated mechanisms with the potential to treat a wide range of tumors. The company has a diverse portfolio of novel programs ranging from early research to investigation in a randomized global study in first-line cancer patients. The company's two novel clinical programs, TPST-1120 and TPST-1495, target PPARα and EP2/EP4, respectively, and are advancing through trials designed to study the agents as monotherapies and in combination with approved agents. Tempest is also developing an orally available inhibitor of TREX1, a target that controls activation of the cGAS/STING pathway. Tempest is headquartered in Brisbane, California. More information about Tempest can be found on the company's website at www.tempesttx.com.

Forward-Looking Statements

This press release 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 availability of data from clinical trials, the favorable results of clinical trials, the ability of the company or its collaborators to present such data at certain conferences, as well as our operational plans. Forward-looking statements are based on information available to Tempest Therapeutics as of the date hereof and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement. These and other risks are described in greater detail in the Form 10-K filed by Tempest Therapeutics with the Securities and Exchange Commission on March 22, 2023. 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. These forward-looking statements should not be relied upon as representing Tempest Therapeutics' views as of any date subsequent to the date of this press release and should not be relied upon as prediction of future events. In light of the foregoing, investors are urged not to rely on any forward-looking statement in reaching any conclusion or making any investment decision about any securities of Tempest Therapeutics.

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[1] If approved by the FDA

[2] Ducreux, et. al., Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021)

[3] Rahib, L. et al. Projecting cancer incidence and deaths to 2030: the undexpected burden of thyroid, liver, and pancreas cancers in the United States. *Cancer Res.* 74, 2913-2921 (2014).

[4] World Health Organization. Liver Cancer Factsheet. Globocan. 2020. Available at: https://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf. Last accessed: April 2023.

[5] Llovet, J. M., Kelley, R. K., Villanueva, A., et al. Hepatocellular carcinoma. Nature Reviews Disease Primers. 2021, 7(1), 6.

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[7] Hack SP, Spahn J, Chen M et al. IMbrave 050: a Phase III trial of atezolizumab plus bevacizumab in high-risk hepatocellular carcinoma after curative resection or ablation. Future Oncology. 2020 May;16(15):975-989.

[8] Saito A, Toyoda H, Kobayashi M et al. Prediction of early recurrence of hepatocellular carcinoma after resection using digital pathology images assessed by machine learning. Modern Pathology. 2021. 34, 417-425.