Tempest Presents Data Supporting the Dual Mechanism of TPST-1495 as an Optimal Approach for Targeting the Prostaglandin Pathway in Cancer

November 12, 2021

- *Data Reported at the 2021 Society for Immunotherapy of Cancer Annual Meeting*

SOUTH SAN FRANCISCO, Calif., Nov. 12, 2021 (GLOBE NEWSWIRE) -- Tempest Therapeutics, Inc. (Nasdaq: TPST), a clinical-stage oncology company developing potentially first-in-class therapeutics that combine both targeted and immune-mediated mechanisms, today reported in vitro and in vivo preclinical data demonstrating the potent dual mechanistic activity of TPST-1495, an orally-available small molecule designed to block the EP2 and EP4 receptors in the prostaglandin (PGE2) pathway. The data show that TPST-1495 effectively promotes anti-tumor activity through both T cell-dependent and -independent mechanisms. TPST-1495 is currently being evaluated in an ongoing Phase 1a/1b dose and schedule optimization trial in patients with solid tumors.

“We’re happy to present these data that build upon existing significant preclinical support for the hypothesis that selectively targeting the EP2 and EP4 receptors together, to the exclusion of EP1 and EP3, is the preferred approach to modulate the prostaglandin pathway for clinical benefit in cancer,” said Tom Dubensky, president of Tempest. “We look forward to generating clinical data as TPST-1495 moves into a mechanism-based combination study with pembrolizumab this quarter, as well as into expansion studies in targeted patient populations in the first half of 2022.”

Presentation Highlights

- TPST-1495 therapy promotes anti-tumor activity through both T cell-independent and T-cell dependent mechanisms, as evidenced by TME infiltration of effector immune cell populations and tumor antigen-specific CD8+ T cells
- TPST-1495 therapy confers a significant survival advantage compared to therapy with single EP2 or EP4 antagonists, or the NSAID Celecoxib, in the $APC^{min/+}$ spontaneous tumor mouse model of CRC
- TPST-1495 confers near complete restoration of immune function including activation of human antigen-specific $CD8^{+}$ T cells in vitro, even in the presence of elevated PGE2 concentrations at which single EP4 or EP2 inhibitors are not effective
- A summary of the near-term clinical development strategy that focuses on patients with histologies known to be prostaglandin-driven, as well as patients with the PIK3CA mutation, a potential biomarker.

Presentation Information

Saturday, November 13, 2021, Hall E, Poster #850

About the PGE2 Pathway and TPST-1495

Elevated expression of COX-2 and overproduction of PGE2 is correlated with progression of diverse malignancies by stimulating tumor cell proliferation via autocrine signaling through the EP2 and EP4 PGE2 receptors, which facilitates survival, evasion and metastasis. PGE2 also suppresses anti-tumor immunity by inhibiting the function of critical anti-tumor immune effector cell populations such as dendritic cells, macrophages, NK cells, and T cells. Recent studies have shown that increased expression of COX-2 and production of PGE2 may play a role in the effectiveness of immune checkpoint inhibitor (“ICI”) therapy and in the development of adaptive immune resistance to ICI therapy.

TPST-1495 is an orally available small molecule designed to block the EP2 and EP4 receptors in the prostaglandin (PGE2) pathway, while sparing the homologous but differentially active EP1 and EP3 receptors. PGE2 signaling through EP2 and EP4 has been observed both to enhance tumor progression and promote immune suppression. Tempest has conducted head-to-head preclinical studies comparing TPST-1495 to single antagonists of EP2 and EP4 and observed significantly enhanced activity of TPST-1495 in both overcoming PGE2-mediated suppression of human immune cells *in vitro*, as well as significantly increased anti-tumor activity in mouse models of human colorectal cancer. Tempest is currently evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and possible anti-tumor activity of TPST-1495 in a multicenter Phase 1a/1b dose and schedule optimization study in subjects with advanced solid tumors, with the potential to expand in indications known to be prostaglandin-driven, including colorectal cancer, or CRC, and in a tumor indication-agnostic, biomarker-selected cohort.

About Tempest Therapeutics

Tempest Therapeutics is a clinical-stage oncology company advancing small molecules that combine both targeted and immune-mediated mechanisms with the potential to treat a wide range of tumors. The company’s two novel clinical programs are TPST-1495 and TPST-1120, antagonists of EP2/EP4 and PPARα, respectively. Both TPST-1495 and TPST-1120 are advancing through Phase 1 studies designed to study both agents as monotherapies and in combination with other approved agents. In collaboration with F. Hoffmann La Roche, TPST-1120 is also advancing through a first line, global, randomized Phase 1b/2 clinical study evaluating TPST-1120 in combination with the standard-of-care regimen of atezolizumab and bevacizumab in patients with advanced or metastatic hepatocellular carcinoma. Tempest is also developing an orally available inhibitor of TREX-1 designed to activate selectively the cGAS/STING pathway, an innate immune response pathway important for the development of anti-tumor immunity. Tempest is headquartered in South San Francisco. 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"). 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, as well as assumptions made by, and information currently available to, management of Tempest. 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", "potentially," and other similar expressions. All statements that are not historical facts are forward-looking statements, including any statements regarding the progress, scope or timing of the development and evaluation in clinical trials of our product candidates or the benefits that may be derived from any future products. Forward-looking statements are based on information available to Tempest 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 as a result of various factors, including, without limitation: our inability to successfully or timely develop our product candidates; our inability to realize any benefits from any future products; and our failure to realize any commercial or market benefit from future products, if any. These and other risks are described in greater detail in the Form 10-Q filed by Tempest with the Securities and Exchange Commission on November 11, 2021. Except as required by applicable law, Tempest 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's 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.

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