Tempest Announces First Patient Dosed with TPST-1495 in Combination with Pembrolizumab

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- *Combination based on both strong mechanistic rationale and preclinical data*

SOUTH SAN FRANCISCO, Nov. 18, 2021 (GLOBE NEWSWIRE) -- Tempest Therapeutics, Inc. (Nasdaq: TPST), a clinical-stage oncology company developing potentially first-in-class therapeutics that combine both tumor-targeted and immune-mediated mechanisms, today announced the first patient has been dosed with TPST-1495 in combination with pembrolizumab in the Phase 1a/1b open-label, dose and schedule optimization study of TPST-1495 in patients with solid tumors.

"We're very pleased to announce the start of patient dosing with TPST-1495 in combination with pembrolizumab," said Sam Whiting, MD, Ph.D., chief medical officer of Tempest. "TPST-1495 is designed to inhibit key components of the Prostaglandin E2, or PGE2, pathway, which is both a driver of tumor cell proliferation and an important suppressor of anti-tumor immune function. In addition, recent data show that PGE2 is involved in enabling tumors to escape from immune checkpoint inhibitors such as pembrolizumab, a process known as adaptive immune resistance. Based on this mechanistic rationale and our preclinical data, we are excited about the potential of this combination to be superior to either approach alone and bring benefit to patients."

The first-in-human Phase 1a/1b, multicenter, open-label, dose and schedule optimization study is being conducted at academic and Phase 1 sites in the U.S. and evaluates TPST-1495 as a single agent and in combination with pembrolizumab to determine its maximum tolerated dose and/or recommended Phase 2 dose, safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary anti-tumor activity in subjects with advanced solid tumors. The preliminary dose-finding stage of the study allows patients with any solid tumor histology, while the study expansion stages are designed both to focus upon patients with prostaglandin-driven cancers, including colorectal cancer, endometrial cancer, squamous cell carcinoma of the head and neck, as well as biomarker-selected patients with tumor-driver mutations in the PIK3CA gene, which are known to enhance the level of prostaglandin production in tumor cells.

About TPST-1495

TPST-1495 is an orally available small molecule designed to block the tumor-promoting EP2 and EP4 receptors in the prostaglandin (PGE2) pathway, while sparing the homologous but immune-supporting 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, pharmacodynamics, and possible anti-tumor activity of TPST-1495 as a single agent and in combination with pembrolizumab in a multicenter Phase 1a/1b dose and schedule optimization study in subjects with advanced solid tumors.

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'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 10, 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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