Tempest Presents Promising Preclinical Data on Two Oncology Programs at the 2022 AACR Annual Meeting

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- Anti-tumor data from systemic novel TREX1 inhibitors designed to activate the STING pathway selectively in tumors
- Additional data further supporting and differentiating TPST-1495, a clinical-stage dual EP2/4 prostaglandin receptor antagonist

SOUTH SAN FRANCISCO, Calif., April 08, 2022 (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 announced the presentation of two poster presentations at the 2022 American Association for Cancer Research (AACR) Annual Meeting reporting new preclinical data that support the company's preclinical TREX1 and clinical TPST-1495 programs.

The first presentation reports on new preclinical data that support TPST-1495, a novel agent designed to specifically block the cancer-promoting EP2 and EP4 prostaglandin E2 (PGE2) receptors, further differentiating TPST-1495 from other approaches targeting the PGE2 pathway. The second presentation reports on proprietary inhibitors of TREX1, a cytosolic DNA exonuclease that inhibits activation of cGAS/STING in tumor and immune cells.

"As part of our diversified pipeline of innovative therapeutics, we reported the first preclinical data from our TREX1 program demonstrating the significant anti-tumor activity of our selective inhibitors. We believe TREX1 is the most promising approach to selectively activate the STING pathway broadly in metastatic disease with systemically administered, small molecule drugs," said Tom Dubensky, Ph.D., president of Tempest. "In addition, we presented preclinical data demonstrating that selective dual antagonism of both EP2 and EP4 prostaglandin receptors with TPST-1495 is a significantly superior approach to provide therapeutic anti-tumor benefit and activate human immune cell populations in vitro, as compared to either single EP2 and EP4 antagonists or NSAIDs. These data support the enthusiasm for our ongoing Phase 1 monotherapy and combination dose escalation and optimization study."

#1333: "Dual Blockade of the EP2 and EP4 PGE2 Receptors with TPST-1495 is an Optimal Approach for Drugging the Prostaglandin Pathway"

In vivo data demonstrated that monotherapy TPST-1495 significantly reduced tumor growth in mice via both T cell-independent and T-cell dependent mechanisms. The anti-tumor effect correlated with direct anti-proliferative effects on tumors in addition to increased tumor infiltration by NK cells, $CD8^+$ T cells, AH1-specific $CD8^+$ T cells, and other anti-tumor myeloid and adaptive immune cell populations. Demonstrating its differentiated potency, therapy with TPST-1495 resulted in a significant survival advantage as compared to therapy with single EP2 or EP4 antagonists, or the NSAID celecoxib, in the $APC^{min/+}$ spontaneous colorectal cancer tumor mouse model. Additional data demonstrated that the administration of TPST-1495 resulted in near-complete restoration of immune function in human immune cell assays, reversing prostaglandin-mediated suppression of lipopolysaccharide stimulation-induced TNF-α production, even in the presence of elevated PGE2 concentrations in which single EP4 or EP2 inhibitors were not effective.

#2075: "Systemic Small Molecule TREX1 Inhibitors to Selectively Activate STING in the TME of Metastatic Disease"

The inaugural presentation for the TREX1 program summarized the approach to develop selective TREX1 inhibitor small molecules with picomolar potency. TREX1 inhibitors were profiled in various human and mouse cell-based assays, demonstrating that inhibition of TREX1 nuclease activity resulted in increased cGAS/STING pathway signaling and production of a reporter or interferon β. The anti-tumor activity of TREX1 inhibitors was evaluated in mice given sub-therapeutic doses of doxorubicin to effect double-stranded breaks in tumor cell DNA and induce the production of TREX1, resulting in significant anti-tumor efficacy and survival.

About TPST-1495

TPST-1495 is an orally available small molecule designed to block the cancer-promoting 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 to enhance tumor progression through the stimulation of tumor proliferation, enhanced angiogenesis and suppression of immune function in the tumor microenvironment. 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 monotherapy and combination therapy 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 TREX1

Genetic evidence from human disease and mouse genetic knock-out studies identify the Stimulator of Interferon Genes (STING) pathway as a critical innate immune sensor for the development of immunity. Tumor cells can evolve to avoid immune recognition through inactivating the STING pathway by diverse mechanisms, indicating that it is important to generating tumor-specific immunity. Selective activation of the STING pathway may be

achieved through targeted inhibition of TREX1, a cytosolic DNA exonuclease that modulates cGAS/STING signaling, which is overexpressed in tumor cells. Tempest is developing TREX-1 inhibitors with oral pharmacokinetics. In vitro and in vivo studies have shown that the company's compounds enhance the activation of the STING pathway in DNA-stimulated human and mouse cells. Furthermore, preclinical results in several tumor models have shown synergies of its TREX-1 compounds with low doses of doxorubicin, demonstrating significant therapeutic anti-tumor efficacy and survival.

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-1120 and TPST-1495, antagonists of PPARα and EP2/EP4, respectively. Both TPST-1120 and TPST-1495 are advancing through Phase 1 clinical trials 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 randomized, global, Phase 1b/2 clinical study in combination with the standard-of-care regimen of atezolizumab and bevacizumab in the first-line treatment of patients with advanced or metastatic hepatocellular carcinoma. Tempest is also developing an orally available inhibitor of TREX-1 designed to activate the cGAS/STING pathway selectively. 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) concerning Tempest Therapeutics, Inc. 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 timing and selection of development candidates, dose selection or commencement of, or availability of data from, clinical trials, or the benefits that may be derived from any future products. 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 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-K filed by Tempest Therapeutics with the Securities and Exchange Commission on March 29, 2022. 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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