Tempest Therapeutics Reports Proof of Mechanism Data for First-in-Class PPAR Alpha Antagonist

--Compelling preclinical data implicate PPAR as a key metabolic checkpoint for tumor growth--

November 13, 2018 08:00 AM Eastern Standard Time

SAN FRANCISCO--(BUSINESS WIRE)--Tempest Therapeutics Inc. presented a poster at the Society for Immunotherapy of Cancer annual meeting in Washington, D.C., describing lead compound TPST-1120's two-pronged mechanism of directly targeting tumor cells dependent on fatty acid metabolism and driving a metabolic shift in the tumor microenvironment to glycolysis from fatty acid oxidation. The resulting significant reductions in tumor growth and stimulation of durable anti-tumor immunity support Tempest's rationale to advance the first-in-class oral small molecule inhibitor of PPAR alpha into clinical studies in patients with advanced solid tumors in early 2019.

The poster titled "Antagonism of Peroxisome Proliferator Activated Receptor Alpha (PPARα) by TPST-1120 Suppresses Tumor Growth and Stimulates Anti-Tumor Immunity" describes studies that demonstrate significant anti-tumor efficacy of TPST-1120. As monotherapy, TPST-1120 prevented fatty acid oxidation and directly inhibited primary human tumor cells in culture and in human tumor xenografts in immune-deficient mice. In tumor-bearing immune-competent animals, TPST-1120 inhibited tumor growth as a single agent and in combination with chemotherapy or with anti-PD-1 antibodies.

For example, TPST-1120 plus gemcitabine significantly increased the long-term survival of mice with pancreatic tumors. TPST-1120 in combination with anti-PD-1 antibodies in mouse models of ovarian and colon cancer showed suppression of tumor growth and complete remissions in some animals. Importantly, cured mice were completely protected against autologous tumor re-challenge in the ovarian model, strongly suggesting immunological T cell memory against the primary tumor.

TPST-1120 elicits its potent anti-tumor effects through direct binding of the PPAR alpha transcription factor, inhibiting the expression of its regulated genes that are critical for fatty acid oxidation. Several malignancies such as hepatocellular carcinoma and renal cell cancer are reliant on fatty acid oxidation. In addition, suppressive immune cells in the tumor microenvironment such as a particular subset of macrophages, regulatory T cells and myeloid-derived suppressor cells all favor fatty acid oxidation. The utilization of fatty oxidation by tumor cells and suppressive immune cells underlines the tumor-intrinsic and tumor-extrinsic anti-tumor properties of TPST-1120.

"Immuno-metabolism is a rapidly evolving field, and it is increasingly recognized that regulating particular metabolic checkpoints that are essential to promote bio-energetic pathways necessary for sustaining tumor growth are important new targets in oncology. Our poster provides the rationale for advancing TPST-1120 into patients with advanced cancers and

also provides insights into the clinical development of this first-in-human molecule," said Tom Dubensky, Ph.D., president and CEO of Tempest.

About Tempest Therapeutics

Tempest Therapeutics is a development-stage biotechnology company advancing small molecules that modulate anti-tumor immunity pathways. The company has a balanced and deep pipeline consisting of first-in-class and potential best-in-class small molecule therapeutics that modulate distinct immune response pathways relevant to mounting an effective anti-tumor response. Tempest's backers include Versant Ventures, F-Prime Capital, Quan Capital, Lilly Asia Ventures, Foresite Capital and Eight Roads Ventures.

Contacts

For Tempest Therapeutics Inc.
Steve Edelson, 415-801-8088
sedelson@versantventures.com