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Peregrine's Vascular Targeting Agent Effective In Combination Cancer Therapy

TUSTIN, Calif., Jun 4, 2003 /PRNewswire-FirstCall via COMTEX/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) announced today the publication of a report showing that certain chemical agents make tumor blood vessels more responsive to its Vascular Targeting Agent (VTA) effector called truncated tissue factor (tTF). Peregrine is developing truncated tissue factor as an anticancer compound that selectively causes blood clots to form within tumor blood vessels, thus cutting off oxygen and nutrients to tumor cells and causing tumor cell death. The new research article was published in the current issue of Arteriosclerosis Thrombosis Vascular Biology.

Pre-clinical data on Peregrine's VTA technology previously published in Science showed that antibodies attached to tTF had dramatic anti-tumor effects. In the Science study, 38% of treated mice had complete tumor regressions. An additional 24% of the mice treated had at least a 50% reduction in tumor mass. In the current published report, tumor blood vessels in animals pre-treated with a chemical agent formed blood clots more easily when administered truncated tissue factor. Blood vessels in normal tissues were not blocked following pretreatment and administration of the tTF. This study indicates that the predisposition of tumor blood vessels toward clotting can be further increased, which could lead to VTA treatments with enhanced safety and efficacy.

The new article, titled "Soluble Tissue Factor Induces Coagulation on Tumor Endothelial Cells In Vivo if Co-Administered With Low-Dose Lipopolysaccharides," concluded that "there are two ways of selective coagulation induction on the surface of intact endothelial cells: (1) via specific antibody directed targeting and (2) via coagulation induction by soluble Tissue Factor (TF) without a functional targeting moiety when additional factors are present that induce local upregulation of endogenous TF and local generation of factor VIIa. Both ways might be exploited for therapeutic approaches in the treatment of cancer." This research was conducted by a third party not affiliated with or supported by Peregrine.

Steven King, Peregrine's president and CEO, said, "This research gives us additional insight into ways to enhance our VTAs in treating cancer. This is important because it further identifies the mechanisms in which truncated tissue factor may create blood clots within tumors. More importantly, it indicates that there may be ways to further enhance the effectiveness of truncated tissue factor-based VTAs without compromising safety."

Philip Thorpe, Ph.D., a co-inventor of the VTA technology, said, "This work indicates that it may be possible to enhance the pro-thrombotic (pro- coagulation) conditions that naturally exist within solid tumors without inducing normal blood vessels to become pro-thrombotic. As a monotherapy, tTF based VTAs achieve almost total occlusion of tumor blood vessels in animal models. By using tTF based VTAs in combination with existing anti-cancer agents, we may be able enhance the safety and efficacy of this treatment approach."

About Truncated Tissue Factor

The blood coagulation cascade (blood clotting) is a normal process that the body uses to stop the flow of blood from damaged tissue. When blood vessels are damaged during injury, factors in the blood come into contact with Tissue Factor (TF) found on cells normally found outside the blood vessels. TF is a receptor protein that is the initiator of the extrinsic pathway of the blood clotting. A truncated derivative of tissue factor (tTF) has been developed by Peregrine in which the portion of the TF molecule that tethers it to the surface of cells has been removed. Since tTF is soluble (not associated with a cell membrane that is necessary for induction of clotting), the tTF is usually inactive when injected into the blood stream. In Peregrine's VTAs, a targeting antibody is substituted for the membrane attachment region of the TF molecule allowing it to be selectively delivered to tumor blood vessel cell surfaces where it can initiate clotting that results in an avalanche of tumor cell death.

About Vascular Target Agents -- The Next Generation of Cancer Therapy

Virtually all detectable tumors rely on a vascular network to obtain oxygen and nutrients, and disruption of this network can have a devastating effect on a tumor. In pre-clinical animal studies, VTAs have shown to be potent anti-cancer agents that act by cutting off the supply of oxygen and nutrients to tumor cells by causing blood clots to form within the tumor's blood supply network. VTAs localize within the tumor vasculature by selectively binding to the flat endothelial cells that line tumor blood vessels. Once the VTA binds to its target, it initiates thrombosis (blood clotting) through a coagulation cascade, which leads to complete clotting of the tumor blood vessels within a matter of minutes. Because blockage of a single capillary results in the destruction of thousands of tumor cells, only a small quantity of VTAs localized in the tumor's vascular system may cause an avalanche of tumor cell death.

Vascular targeting agents offer several advantages as potentially powerful anti-cancer treatments. By targeting receptors unique to tumor cell vasculature, VTAs can kill tumors by cutting off oxygen and nutrients without causing damage to surrounding healthy tissue. Additionally, VTAs reduce the risk of potential side effects by operating at lower dosages than traditional cancer therapies because they do not need to penetrate the innermost layer of a tumor to take effect. Lastly, while drug resistance caused by the instability and mutability of cancer cells is a significant problem with conventional therapies that target tumor cells, cells targeted by VTAs do not mutate to become drug resistant.

About Peregrine Pharmaceuticals

Peregrine Pharmaceuticals is a biopharmaceutical company focused on the development, commercialization and licensing of unique technologies for the treatment of cancer, primarily based on three collateral targeting technologies. Peregrine's Tumor Necrosis Therapy (TNT), Vasopermeation Enhancement Agents (VEA), and Vascular Targeting Agents (VTA) technologies target cell structures and cell types that are common among solid tumor cancers, giving them broad applicability across various tumor types. The company has received approval from the FDA to start a Cotara™ Phase III clinical trial for brain cancer. Cotara is also being studied in a Phase I trial for colorectal, pancreas, soft tissue sarcoma and biliary cancers at Stanford University. The company is focused on licensing collaborations for all of its technologies under development. The company's Oncolym® technology to treat non-Hodgkin's B-cell lymphoma is in Phase I/II of development is available for licensing. The company also operates a cGMP contract manufacturing facility for monoclonal antibodies and recombinant proteins through its wholly owned subsidiary Avid Bioservices, Inc. (www.avidbio.com). Copies of Peregrine press releases, SEC filings, current price quotes and other valuable information for investors may be found on the website www.peregrineinc.com.

Safe Harbor Statement: This release may contain certain forward-looking statements that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Actual events or results may differ from the company's expectations as a result of risk factors discussed in Peregrine's reports on file with the U.S. Securities and Exchange Commission, including, but not limited to, the company's report on Form 10-K for the year ended April 30, 2002 and on Form 10-Q for the quarter ended January 31, 2003.

Investor Relations Contact
Frank Hawkins and Julie Marshall
Hawk Associates, Inc.
(800) 987-8256 or
info@hawkassociates.com

SOURCE Peregrine Pharmaceuticals, Inc.

Investor Relations, Frank Hawkins or Julie Marshall, both of
Hawk Associates, Inc., +1-800-987-8256, or info@hawkassociates.com, for
Peregrine Pharmaceuticals

http://www.peregrineinc.com