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## Targeted Delivery of Tissue Factor Research Published in 'Cancer Research'

TUSTIN, Calif., Sep 18, 2003 /PRNewswire-FirstCall via COMTEX/ -- Peregrine Pharmaceuticals, Inc. (Nasdaq: PPHM) announced today the publication of a report in the current issue of "Cancer Research" showing that different antibody-based targeting agents can be used to effectively deliver the coagulation protein truncated tissue factor (tTF) to tumors for the treatment of cancer. The study also highlights the effectiveness of delivering agents to tumors that block blood flow to the tumor resulting in therapeutic effects, which is the concept behind Peregrine's Vascular Targeting Agent (VTA) technology. Peregrine has been researching the use of truncated tissue factor as an anti-cancer 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.

In the report, truncated tissue factor was linked to several antibodies that target tumors or tumor vasculature. The targets studied included markers of tumor blood vessels and structures found in the necrotic core of solid tumors. Tumor blood vessels were selectively blocked by the antibody targeted tissue factor while vessels in normal tissues remained open. In the study the tumors turned black within hours and regressed in size rapidly which has been observed in other tTF treatments. The results of the study demonstrated a significant therapeutic effect in lung and colon carcinoma tumor models. Pre-clinical data on Peregrine's VTA technology previously published in "Science" showed that antibodies attached to tTF also had significant 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.

Alan Epstein, M.D., Ph.D., professor of pathology at the Keck School of Medicine of the University of Southern California (USC), the inventor of Peregrine's Tumor Necrosis Therapy (TNT) targeting platform and a co-author on the new published report, said, "This work further indicates the potential of truncated tissue factor as a therapeutic agent for tumor therapy and a potential new use of the TNT targeting platform. The new article and our prior research experience demonstrates that multiple targets exist which can be used to localize tTF to occlude tumor blood vessels."

### 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. Using 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 in Phase I/II of development is available for licensing. The company operates a cGMP contract manufacturing facility for monoclonal antibodies and recombinant proteins through its wholly-owned subsidiary Avid Bioservices, Inc. ([www.avidbio.com](http://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](http://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-Q for the quarter ended July 31, 2003 and on Form 10-K for the year ended April 30, 2003.

Contact:

Peregrine Investor Relations  
Frank Hawkins and Julie Marshall  
Hawk Associates, Inc.  
(800) 987-8256 or  
[info@hawkassociates.com](mailto:info@hawkassociates.com)

SOURCE Peregrine Pharmaceuticals, Inc.

Investor Relations, Frank Hawkins, or Julie Marshall, both of Hawk Associates, +1-800-987-8256, or [info@hawkassociates.com](mailto:info@hawkassociates.com), both for Peregrine Pharmaceuticals

<http://www.peregrineinc.com>