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## **Peregrine's Vascular Targeting Agent Technology Reviewed In 'Clinical Cancer Research'**

TUSTIN, Calif., Feb 6, 2004 /PRNewswire-FirstCall via COMTEX/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) announced today that a review of various Vascular Targeting Agent (VTA) technologies has been published in "Clinical Cancer Research." The review, titled "Vascular Targeting Agents as Cancer Therapeutics" was written by Philip E. Thorpe, Ph.D. Dr. Thorpe, a scientific consultant to Peregrine, is the co-inventor of Peregrine's VTA technology and is one of the world's leading experts and pioneers in the VTA field.

Vascular Targeting Agents work by cutting off blood flow into solid tumors. By shutting off the blood flow, the tumor cells no longer receive oxygen and nutrients resulting in widespread death and decay of tumor cells within the tumor. Since the blood vessels in different solid tumors will have similar characteristics, it is believed that a single VTA will be able to treat a variety of different tumor types.

In the article, Dr. Thorpe stated, "The potential of vascular targeting as a cancer therapeutic approach has been firmly established in experimental studies. The VTAs all lead to rapid reductions in tumor blood flow and extensive necrosis in experimental tumors. They have also been shown to be more effective in large rather than small tumors. Tumor stabilizations are commonly seen in preclinical models, and in combination with anti-proliferative modalities, where lasting tumor regressions are obtained. The preliminary demonstration of tolerability in humans supports the continued development of vascular targeting as a novel cancer therapeutic approach. The tolerability profiles seen and the demonstration of monotherapy efficacy are exciting for the future development of combined modality regimens."

Peregrine has built a comprehensive patent portfolio around the concept of Vascular Targeting Agents. This intellectual property portfolio includes broad patents that cover the concept of targeting tumor blood vessels in order to deliver a therapeutic or diagnostic agent to the tumor. Peregrine currently has several research programs and commercial licensing arrangements for the development of ligand directed VTAs for the treatment and diagnosis of cancer. In addition, the company is in active discussions with other biotechnology and pharmaceutical companies to move additional VTA development programs forward.

VTAs can be broadly divided into two types, small molecule VTAs and ligand-directed VTAs. Small molecule VTAs do not localize selectively to tumor vessels but exploit pathophysiological differences between tumor and normal tissue endothelium to achieve selective occlusion of tumor vessels. These differences in tumor compared with normal tissue endothelial cells include their increased proliferation, permeability, and reliance on a tubulin cytoskeleton to maintain cell shape. In contrast, ligand-based VTAs use a targeting ligand to achieve selectivity of binding to and occluding tumor vasculature. The two types are grouped together because they both cause acute vascular collapse in tumors, which leads to massive central necrosis.

VTAs differ conceptually from anti-angiogenic agents, which prevent the growth of new blood vessels in tumors. While anti-angiogenesis agents prevent the spread and growth of tumors, VTAs are most effective at destroying the existing tumor mass. It is believed that the two approaches represent synergistic mechanisms of action and that they may eventually be used in combination.

Peregrine has over 60 issued, allowed or pending patents around Vascular Targeting Agents. This broad intellectual property includes among other things markers expressed, induced or otherwise associated with tumor vasculature, linkers for joining a targeting moiety to an effector moiety and effectors capable of damaging the tumor vasculature including toxins, cytotoxic agents, radioisotopes and coagulation proteins. These patents provide opportunities for the development and licensing of VTAs to multiple strategic partners. These potential partners include biotechnology and pharmaceutical companies with proprietary vascular targets or companies with proprietary effectors that they would like to target to tumor vasculature. Examples of these types of licensing arrangements include licensing agreements with Schering AG for vascular targeted imaging applications and with SuperGen, Inc. for VTAs targeted using Vascular Endothelial Growth Factor. The company is also actively engaged in internal development and discussions with other companies in areas outside of oncology, including ocular disease and arthritis."

The concept behind vascular targeting agents is to selectively target and destroy the endothelium (blood vessels) of solid tumors that results in the death of tumor cells caused from the lack of oxygen and nutrients. VTAs halt the blood flow in most of the vessels in the tumor, resulting in the widespread necrosis of established tumors. VTAs differ conceptually from anti-angiogenic agents, which prevent the process of new blood vessel formation from existing vessels. VTAs produce a characteristic pattern of widespread central necrosis in experimental tumors, which can extend to as much as 95% of the tumor.

VTAs are most effective against vessels in the interior of the tumor, possibly because the high interstitial pressure in these regions contributes to vascular collapse. In contrast, many direct-acting anti-tumor therapies are most effective against the rapidly dividing tumor cells in the well-oxygenated periphery of the tumor. Angiogenesis inhibitors are also most effective against tumor cells in the tumor periphery where angiogenesis occurs most vigorously. Combining VTAs with anti-proliferative anti-tumor therapies or angiogenesis inhibitors can lead to additive or synergistic activity in experimental solid tumors.

#### 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™ registration clinical trial for brain cancer. Cotara is also being studied in a Phase I trial for colorectal cancer 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, Peregrine's report on Form 10-Q for the quarter ended October 31, 2003 and on Form 10-K for the year ended April 30, 2003.

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