



November 13, 2002

## **Peregrine's Anionic Phospholipid Based Vascular Targeting Agent Technology Published in Cancer Research**

TUSTIN, Calif., Nov. 13 /PRNewswire-FirstCall/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) announced today that researchers at the University of Texas Southwestern Medical Center at Dallas (UT Southwestern) have further characterized and defined anionic phospholipids as potential markers for tumor blood vessels. Researchers at UT Southwestern, through a Peregrine sponsored research collaboration, have developed monoclonal antibodies that target anionic phospholipids to be used as potential Vascular Targeting Agents (VTA). Antibodies which selectively target anionic phospholipids have been exclusively licensed to Peregrine from the University of Texas System.

The study, which appears in the November issue of *Cancer Research*, determined that anionic phospholipids become exposed on tumor vasculature. The study used several monoclonal antibodies which selectively target anionic phospholipids to show that anionic phospholipids are exposed on tumor blood vessels but not on normal blood vessels. The study also evaluated known tumor-associated conditions which may be responsible for the unusual expression of anionic phospholipids on the surface on tumor blood vessels. The results of this study give us a greater understanding of the mechanisms that control the exposure of anionic phospholipids on the surface of cells.

Peregrine President and CEO Edward J. Legere, said, "We believe this is another important step forward in our understanding of the potential value of using anionic phospholipids as specific targets for VTAs to be used in the fight against cancer. We believe anionic phospholipids are attractive targets for our VTA platform. We are currently developing chimerized and fully human monoclonal antibodies that target anionic phospholipids as potential clinical candidates. We look forward to continuing to collaborate with UT Southwestern to advance these important VTA compounds into human clinical studies."

Anionic phospholipids are attractive as tumor blood vessel targets for several reasons: they are abundant; they are on the luminal (blood) surface of tumor endothelium (blood vessel), which is directly accessible for binding by VTAs in the blood; they are present on a significant percentage of tumor endothelial cells in diverse solid tumors; and they appear to be absent from endothelium in all normal tissues.

The main function of phospholipids is the formation of cellular membranes. In normal cells, anionic phospholipids are on the inside of the cellular membrane. Exposure of anionic phospholipids on the cell surface occurs during apoptosis (normal cell death), necrosis, cell injury, cell activation and malignant transformation. Factors in the tumor microenvironment cause a break down of asymmetry and exposure of anionic phospholipids on the cell surface of the blood vessel and malignant cells.

### 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, Inc.

Peregrine Pharmaceuticals is a biopharmaceutical company focused on the development, commercialization and licensing of unique technologies for the treatment of cancer, primarily based on its three "collateral targeting technologies." Peregrine's

Tumor Necrosis Therapy (TNT), Vasopermeation Enhancement Agents (VEA), and Vascular Targeting Agents (VTA) target cell structures and cell types that are common among solid tumor cancers, giving them broad applicability across various tumor types. The company's lead TNT anti-cancer drug, Cotara™, is currently in a multicenter Phase II clinical trial for brain cancer and Phase I trials for colorectal, pancreas, soft tissue sarcoma and biliary cancers. The company also operates a growing 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-K for the year ended April 30, 2002 and on Form 10-Q for the quarter ended July 31, 2002.

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