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## **Peregrine's Phosphatidylserine-Based Vascular Targeting Agent Technology Published In International Journal of Radiation - Oncology - Biology - Physics**

TUSTIN, Calif., Dec. 9 /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 the anionic phospholipid phosphatidylserine (PS) as a potential marker for tumor blood vessels to be used for cancer imaging and therapy. Researchers at UT Southwestern, through a Peregrine sponsored research collaboration, have developed monoclonal antibodies that target phosphatidylserine to be used as potential Vascular Targeting Agents (VTA). Antibodies which selectively target phosphatidylserine for targeting cancer have been exclusively licensed to Peregrine from the University of Texas System.

The study, which appears in the December issue of International Journal of Radiation Oncology - Biology - Physics, determined that phosphatidylserine becomes exposed on tumor vasculature in various solid tumors in mice. In addition, the study investigated the potential causes of PS translocation to the surface to the tumor blood vessel. Phosphatidylserine is almost exclusively found on the internal side of the plasma membrane of cells. The results of this study validate PS as a specific marker for tumor vasculature and give us a greater understanding of the mechanisms that control the exposure of PS on the surface of tumor blood vessels.

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, and phosphatidylserine in particular, as specific targets for VTAs to be used in the fight against cancer. We believe phosphatidylserine is an attractive target for our VTA platform. We are currently developing chimerized and fully human monoclonal antibodies that target phosphatidylserine and other anionic phospholipids as potential clinical candidates. We look forward to our continuing collaboration with UT Southwestern to advance these important VTA compounds."

Phosphatidylserine is attractive as a tumor blood vessel target for several reasons: it is abundant (approximately 3,000,000 molecules per tumor cell); it is on the luminal (blood) surface of tumor endothelium (blood vessel), which is directly accessible for binding by VTAs in the blood; it is present on a significant percentage of tumor endothelial cells in diverse solid tumors; and it appears to be absent from endothelium in all normal tissues.

The main function of phosphatidylserine and other phospholipids is the formation of cellular membranes. In normal cells, anionic phospholipids, including phosphatidylserine, are on the inside of the cellular membrane. Exposure of phosphatidylserine 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 phosphatidylserine on the cell surface of the blood vessel and malignant cells.

### **About Vascular Targeting 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 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 is working closely with the FDA on the lead TNT anti-cancer drug, Cotara™, to obtain approval of Phase III clinical trial protocol 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 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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