



February 3, 2003

## **Peregrine's Anti-Angiogenesis Antibody, 2C3, Shown to Inhibit Tumor Growth by 75%**

TUSTIN, Calif., Feb 3, 2003 /PRNewswire-FirstCall via COMTEX/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) said today that researchers at the University of Texas Southwestern Medical Center at Dallas (UT Southwestern) have published data detailing the anti-tumor effects of the 2C3 antibody. The study, which appears in the most recent issue of *Angiogenesis*, demonstrated that administration of 2C3 to tumor-bearing mice inhibited tumor growth by 75%, as compared to a control group.

2C3 is an antibody that blocks the interaction of Vascular Endothelial Growth Factor (VEGF) with one of its key receptors. VEGF is a primary stimulant of tumor angiogenesis. Researchers at UT Southwestern, through a Peregrine sponsored research collaboration, have developed a monoclonal antibody (2C3) that blocks VEGF from binding to VEGF receptor 2 (KDR/Flk-1) but not VEGF receptor 1 (FLT-1/flt-1). 2C3 has been exclusively licensed to Peregrine from the University of Texas System.

In a metastatic breast cancer model, treatment of 2C3 also inhibited the establishment of tumor colonies and reduced tumor burden in the lungs of mice injected intravenously with human breast cancer cells. Of particular interest, 2C3 also inhibited the expression of VEGF receptor 2. This dual effect further inhibits the ability of cancer cells to use VEGF to grow tumor vessels. No toxicity was observed in any of these studies. The authors of the study suggest that 2C3 is a candidate for treating primary cancer and for preventing the outgrowth of tumor metastases in cancer patients.

Inhibiting VEGF receptor 2, but not VEGF receptor 1, is key in the anti-tumor activity of 2C3. VEGF receptor 2 has been shown to be the main receptor that cancer cells use to grow new vessels, whereas VEGF receptor 1 is utilized for normal cellular function of macrophages and monocytes. An inhibitor of VEGF that selectively blocks the function of VEGF receptor 2 should not interfere with macrophage infiltration into tumors, which is an important part of the body's defenses against cancer. This is potentially a major advantage of 2C3 over other VEGF inhibitors that block VEGF binding to both receptors.

Peregrine president and CEO Edward J. Legere said, "Peregrine and its researchers continue to make significant progress in the discovery and development of novel compounds that can be used to treat cancer while trying to minimize the side effects that usually accompany existing treatments. The ability to block a main receptor that cancer cells use to grow new blood vessels while at the same time not inhibiting a receptor that is used by the body to naturally fight cancer is potentially a very important development. We are currently developing a fully human antibody for this technology that can be evaluated for use in human clinical studies. The 2C3 antibody and other proprietary VEGF antibodies are available for licensing for use as Vascular Targeting Agents."

The 2C3 antibody is being developed as part of Peregrine's Vascular Targeting Agent (VTA) program, which works by attacking the blood supply of solid tumor cancers as a means to destroy the tumor.

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

Virtually all detectable tumors rely on a vascular network to obtain oxygen and nutrients. 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.

VTAs 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 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 October 31, 2002.

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