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## **Peregrine Pharmaceuticals Announces Grant of Broad Claims in Europe for its Vascular Targeting Agent Technology**

TUSTIN, Calif., March 23 /PRNewswire-FirstCall/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) announced today the grant of European Patent EP0627940B1 with broad claims covering the company's Vascular Targeting Agent (VTA) technology platform. Specifically covered by the newly granted patent are VTAs that use antibodies to deliver therapeutic or diagnostic agents to tumor blood vessels. The new patent covers a wide number of VTAs each of which may use a different combination of blood vessel targets and effectors for cancer therapy or diagnosis. The claims in the newly granted patent extend to Europe the broad patent coverage that was granted in the U.S. by patent number 6,051,230, which was issued in 2000. Peregrine's VTA technology platform was invented in the laboratory of Philip Thorpe, Ph.D. at the University of Texas Southwestern Medical Center at Dallas (UT Southwestern). The VTA technology is being developed by Peregrine under an exclusive worldwide licensing agreement with The University of Texas System.

Peregrine President and CEO Steven King stated, "The grant of this broad European patent is a major milestone for our VTA technology platform. This patent significantly strengthens our intellectual property position in the VTA field. Peregrine's VTA patent portfolio may potentially provide significant protection for our existing licensing agreements in the VTA area with Schering AG and SuperGen, Inc. In addition, given the broad claims granted under these patents, we believe there will be substantial licensing and co-development opportunities for compounds that may fall under and benefit from our VTA patent protection."

Peregrine's VTA patent estate includes more than 190 issued or pending patents and patent applications. Specifically covered by the newly granted patent are VTAs for cancer therapy or diagnosis using antibodies or antibody fragments that bind to blood vessel markers that are expressed on, accessible to binding on or localized on tumor blood vessels. In addition to the broad coverage of vascular targeting agents, the new patent also covers targeting antibodies or antibody fragments linked to a wide variety of therapeutic agents including but not limited to, chemotherapeutic agents, biologic agents, coagulants, toxins and radioisotopes. Peregrine's business development philosophy in the VTA field is to grant access to companies interested in actively developing VTAs. The company has entered into both exclusive and non-exclusive licenses for different targets and/or effectors to meet the needs of our licensees.

### About Vascular Targeting Agents

VTAs developed by Dr. Thorpe and his team represent the next generation of cancer therapy that works by a novel mechanism of action. Essentially, all detectable tumors rely on blood vessels to obtain oxygen and nutrients. Peregrine's 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 occludes the tumor vessels. 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.

There are thought to be a number of advantages of VTAs over other cancer therapies making them 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 part 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, the cells targeted by VTAs do not mutate to become drug resistant. Peregrine believes that VTAs will be most effective when used in combination with existing anti-cancer therapies, providing a powerful "1-2 punch" for the effective treatment of various solid tumor cancers.

Two types of VTAs are currently being developed for cancer treatment: ligand-directed and small molecule VTAs. Ligand-directed VTAs use antibodies and peptides to selectively target toxins, pro-coagulants, and pro-apoptotic effectors specifically to tumor endothelium. Most small molecule VTAs do not specifically localize to tumor endothelium, but exploit pathophysiological differences between tumor and normal tissue endothelia to induce selective occlusion of tumor vessels. Both approaches have shown promise in pre-clinical animal testing. The key difference in the two technologies is that most ligand-directed VTAs (Peregrine's patented approach) require one or only a few doses to cause irreparable harm to the tumor blood vessel network, whereas, many small molecule based VTAs require multiple or chronic dosing regimens to provide the same effect.

Both types of VTAs have produced a characteristic pattern of necrosis after administration to mice and rats with solid tumors. They cause a widespread central necrosis that can extend to as much as 95% of the tumor. A thin rim of viable tumor cells usually survives at the periphery of the tumor at which point the tumor cells obtain nutrients from unaffected blood vessels in the surrounding normal tissues. These tumor cells at the periphery of the solid tumor can usually be treated effectively with existing chemotherapy agents.

About Peregrine Pharmaceuticals, Inc.

Peregrine's research and development efforts focus on discovering and developing products that affect blood flow to tumors. Peregrine's vascular research programs fall under several different proprietary platforms including Anti-Phospholipid Therapy (APT), Vascular Targeting Agents (VTAs), anti-Angiogenesis and Vasopermeation Enhancement Agents (VEAs). The company has research collaborations with pharmaceutical and biotechnology companies to develop its VTA platform for therapeutic and diagnostic applications and expects to enter its first APT compound into clinical trials for cancer therapy during calendar year 2004.

Peregrine's vascular agents may also have applications in other angiogenesis-dependent diseases besides cancer such as diabetes, arthritis, skin disorders and eye diseases. Peregrine currently has exclusive rights to over 190 U.S. and foreign patents and patent applications that broadly cover its vascular programs. In addition, the company is currently evaluating its proprietary technology for use in treating non-angiogenesis dependent diseases such as viral infections. The company believes that the pre-clinical data generated by the company and the broad nature of its intellectual property may provide many opportunities for product development, partnering and licensing.

Peregrine's most clinically advanced therapeutic program is based on a targeting platform outside vascular biology. This technology platform is known as Tumor Necrosis Therapy (TNT) and targets dead or dying tumor cells that are common to the majority of different tumor types. Cotara™, the most clinically advanced TNT program, is currently in a Phase I clinical trial for the treatment of colorectal carcinoma at Stanford University Medical Center. In addition, we have received protocol approval from the U.S. Food and Drug Administration ("FDA") to initiate a registration clinical study for the treatment of brain cancer. The company is currently seeking a development or funding partner to move the brain cancer program forward. The company believes that continuing the clinical development of Cotara™ in tumor types other than brain cancer will add significant value to the program. The company has a research collaboration to develop immunocytokines based on the TNT platform and a TNT based agent has been developed and approved for the treatment of lung cancer in China under a licensing agreement.

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)). Avid produces clinical trial materials to support Phase I through phase III clinical trials for biotechnology companies including Peregrine. 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 January 31, 2004 and on Form 10-K for the year ended April 30, 2003.

SOURCE Peregrine Pharmaceuticals, Inc.

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