May 21, 2003

Peregrine's Vasopermeation Enhancement Agent Technology Published In Journal Of The National Cancer Institute

TUSTIN, Calif., May 21 /PRNewswire-FirstCall/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) announced today that researchers from the Keck School of Medicine of the University of Southern California (USC) have isolated a protein fragment derived from the cancer immunotherapy drug interleukin 2 (IL-2) that functions to significantly enhance the uptake of chemotherapeutic agents by tumor cells by up to 400%. This technology is part of a class of compounds called Vasopermeation Enhancement Agents (VEA) being developed by Peregrine. Researchers at USC, through a Peregrine-sponsored research collaboration, developed the VEA technology. The VEA technology has been exclusively licensed from USC to Peregrine.

This research was described in the paper "Permeability Enhancing Peptide (PEP) -- A Protein Fragment of Interleukin-2 Responsible for Vasopermeability" which was published in the May 21, 2003 issue of the Journal of the National Cancer Institute.

According to Alan Epstein, M.D., Ph.D., professor of pathology at the Keck School of Medicine and, along with other researchers at USC, author of the paper, "When this patented protein fragment is attached to a tumor-targeting antibody, it can prompt tumor cells to soak up almost 400 percent the normal amount of chemotherapy drugs. It does this by making the tumor's blood vessel walls more open or permeable to the drugs." (Blood vessel walls are made of endothelial cells that are usually tightly joined together; when the junctions between those cells loosen up, it becomes easier for molecules to enter or leave the bloodstream.) "We've showed that PEP can be used to induce selective and reversible blood vessel permeability at the tumor site to get better drug uptake. This may turn out to be a hugely important tool in cancer therapy."

"This publication represents an important validation of the VEA technology platform," stated Steven King, president and CEO of Peregrine. "We are very excited about the clinical potential of the VEA platform based on the data presented in this publication and unpublished data generated by Peregrine. We are continuing with our pre-clinical development of a fully human VEA clinical candidate which utilizes the PEP technology for evaluation in future human clinical trials."

About Interleukin-2

Interleukin-2 (IL-2) is a naturally occurring cytokine, which is produced by helper T lymphocytes. Cytokines are proteins in the body that stimulate and regulate the immune system. Interleukin-2 is an important cytokine and occupies a central role in the augmentation of cell-mediated immune response. In addition to its cytokine activity, IL-2 has been shown to contain a domain, which produces vascular permeability when administered systemically (capillary leak syndrome). When IL-2 is used in a clinically effective dose for the treatment of cancer, it causes massive leaking of blood outside of the vascular network. This toxic side effect has limited the clinical effectiveness of IL-2 for the treatment of cancer.

About Permeability Enhancing Peptide

The goal of USC/Peregrine's research on IL-2 was to develop a drug compound that had the ability to induce vasopermeation at, and only at, the tumor site. To achieve this, scientists at USC/Peregrine mapped out the structure of IL-2 and identified the region that is responsible for causing capillary leak syndrome. This region was then synthesized and tested for suitability as a vasopermeability agent. Preclinical studies showed this region has 100% of the vasopermeability activity of intact IL-2 but lacked its cytokine activity. This proprietary new compound is called Permeability Enhancing Peptide (PEP) and has been patented by USC and exclusively licensed to Peregrine. By attaching PEP to a monoclonal antibody that targets tumors, vasopermeability can be localized only at the tumor site.

About Vasopermeation Enhancement Agents

Barriers to Existing Cancer Therapies

Most traditional approaches to cancer therapy attempt to destroy individual cancer cells. Drugs that target cancer cells must overcome a significant number of structural barriers within the tumor in order to be effective. They must first exit the tumor blood vessels, migrate past the support structures that underlie the vessels and eventually make their way to the cancer cells. As result of these structural barriers, very little drug injected into the blood stream of a patient is able to reach and destroy

cancer cells. One potential solution to this problem is to increase the permeability of the blood vessels within the tumor, which will permit more therapeutic drug to reach and kill substantially more cancer cells.

Mechanism of Action

Vasopermeation Enhancement Agents are a new class of drugs, which are designed to increase the uptake of cancer therapeutics and imaging agents at the tumor site, potentially resulting in greater efficacy. VEAs work by using monoclonal antibodies, or other biologically active targeting agents, to deliver known vasoactive compounds (i.e. molecules that cause tissues to become more permeable) selectively to solid tumors. Once localized at the tumor site, VEAs alter the physiology and the permeability of the vessels and capillaries that supply the tumor. In pre-clinical studies, drug uptake has been increased up to 400% in solid tumors when VEAs were administered several hours prior to the therapeutic treatment. VEAs are intended to be used as a pre-treatment for most existing cancer therapies and imaging agents. VEAs may be effective across multiple tumor types.

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™ Phase III clinical trial 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's Oncolym® technology to treat non-Hodgkin's B-cell lymphoma is in Phase I/II of development is available for licensing . 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). 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.

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 January 31, 2003.

Investor Relations Contact
Frank Hawkins and Julie Marshall
Hawk Associates, Inc.
(800) 987-8256 or
info@hawkassociates.com

SOURCE Peregrine Pharmaceuticals, Inc.

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/CONTACT: Frank Hawkins or Julie Marshall, both of Hawk Associates, Inc., +1-800-987-8256, or info@hawkassociates.com, for Peregrine Pharmaceuticals, Inc./

/Web site: http://www.peregrineinc.com /

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