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Peregrine's Vasopermeation Enhancement Agent Technology Highlighted In Nature Reviews Cancer

TUSTIN, Calif., June 23 /PRNewswire-FirstCall/ -- Peregrine Pharmaceuticals (Nasdaq: PPHM) said today that part of its Vasopermeation Enhancement Agents (VEA) technology was highlighted in a commentary article published in the July 2003 issue of Nature Reviews Cancer. The original article on the discovery of the portion of the immunotherapy drug interleukin 2 (IL-2) responsible for permeability enhancement was published by researchers from the Keck School of Medicine of the University of Southern California (USC) in the Journal of the National Cancer Institute in May. Researchers at USC, through a Peregrine sponsored research collaboration, developed the VEA technology which has been exclusively licensed from USC to Peregrine. The VEA technology is currently being developed for commercial applications by Peregrine.

"Our research on the IL-2 molecule may someday yield several important anti-cancer compounds," said Alan Epstein, M.D., Ph.D., professor of pathology at the Keck School of Medicine. "The portion of the IL-2 molecule responsible for enhancing permeability, which we have termed 'PEP' for Permeability Enhancing Peptide, can prompt tumors to soak up almost three times the normal amount of chemotherapy drugs and can improve the efficacy of the administered drugs when attached to a tumor-targeting antibody. This may provide a new way of enhancing the delivery and efficacy of existing chemotherapeutic drugs for the treatment of cancer."

"We are pleased that the discovery of the PEP molecule has been reviewed in Nature indicating the importance of the earlier publication," said Steven King, president and CEO of Peregrine. "We are continuing 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 has been to develop a drug compound with 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 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 in Phase I/II of development is available for licensing. The company 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.

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