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**PHARMACYCLICS ANNOUNCES *CANCER RESEARCH* PUBLICATION  
DEMONSTRATING NOVEL ANTI-CANCER ACTIVITY OF XCYTRIN**

**Sunnyvale, Calif. -- May 2, 2005** -- Pharmacyclics, Inc. (Nasdaq: PCYC) today announced that *Cancer Research*, the journal of the American Association for Cancer Research (AACR), published a study that further characterizes the mechanism of action of Xcytrin<sup>®</sup> (motexafin gadolinium) Injection and provides better understanding of the drug's unique anti-cancer properties. The study was conducted by scientists from the Institute for Genetic Medicine at the University of Southern California and the Department of Radiation Oncology at the University of Pennsylvania in collaboration with Pharmacyclics.

“We found that cancer cells treated with Xcytrin upregulate several genes, including many involved in regulation of oxidative stress and zinc ion metabolism,” stated Joseph G. Hacia, Ph.D., Assistant Professor, Biochemistry and Molecular Biology, Institute for Genetic Medicine, Keck School of Medicine of the University of Southern California. “Our studies showed that Xcytrin induces oxidative stress in cancer cells and this leads to disruption of zinc metabolism and alteration of key enzymes and metabolites necessary for normal cellular function.”

In order to gain a better understanding of the mechanism of action of Xcytrin, researchers conducted a series of gene expression profiling analyses and biochemical studies on human lung, prostate and lymphoma cancer cell cultures treated with Xcytrin. The researchers found that drug treatment elicited a highly specific response that manifested

in elevated levels of metallothionein isoforms and zinc transporter 1 transcripts. Metallothioneins are a family of proteins that respond to oxidative stress and act as chaperones for zinc ions. Intracellular free zinc levels increased in response to treatment with Xcytrin in the absence of exogenous zinc, indicating that Xcytrin can mobilize bound intracellular zinc. Zinc plays a fundamental role in protein assembly, structure and function, and levels of zinc, and its trafficking within cells, are precisely regulated. Zinc can directly inhibit an enzyme known as thioredoxin reductase, which plays a fundamental role in a wide range of cellular activities including biosynthesis, replication and survival. In this study, researchers showed that the enzyme activity of thioredoxin reductase was inhibited in cancer cells treated with Xcytrin. The authors indicate that Xcytrin may have multiple targets for its activity within the cancer cell, which result in oxidative stress and impairment of metabolism.

“These findings further elucidate Xcytrin’s unique properties and support the potential use of Xcytrin in a broad range of cancers,” said Richard A. Miller, M.D., president and chief executive officer of Pharmacyclics. “We believe Xcytrin is representative of a new class of anti-cancer agents that selectively target multiple biochemical pathways relevant to cancer.”

### **About Xcytrin**

Pharmacyclics is developing Xcytrin as an anti-cancer agent with a novel mechanism of action that is designed to selectively concentrate in tumors and induce apoptosis (programmed cell death). Pharmacyclics has been granted Fast-Track status by the U.S. Food and Drug Administration (FDA) for Xcytrin for the treatment of brain metastases (cancer that has spread to the brain from another part of the body) in non-small cell lung cancer (NSCLC) patients. Xcytrin is currently being evaluated in a randomized Phase 3 clinical trial (the SMART trial) that recently completed enrollment and is designed to compare the effects of whole brain radiation therapy (WBRT) alone to WBRT plus

Xcytrin for the treatment of brain metastases in patients suffering from NSCLC. Xcytrin also is currently under investigation in several Phase 1 and Phase 2 clinical trials in various cancers evaluating its use as a single agent and in combination with chemotherapy and/or radiation therapy.

### **About Pharmacyclics**

Pharmacyclics is a pharmaceutical company developing innovative products to treat cancer and atherosclerosis. The company's products are rationally designed, ring-shaped small molecules called texaphyrins that are designed to selectively target and disrupt the bioenergetic processes of diseased cells, such as cancer and atherosclerotic plaque. More information about the company, its technology, and products in development can be found on its website at [www.pyc.com](http://www.pyc.com). Pharmacyclics<sup>®</sup>, Xcytrin<sup>®</sup> and the "pentadentate" logo<sup>®</sup> are registered trademarks of Pharmacyclics, Inc.

**NOTE:** Other than statements of historical fact, the statements made in this press release about enrollment plans for our clinical trials, progress of and reports of results from preclinical and clinical studies, including results from our SMART trial, clinical development plans and product development activities are forward-looking statements, as defined in the Private Securities Litigation Reform Act of 1995. The words "believe," "will," "continue," "plan," "expect," "intend," "anticipate," variations of such words, and similar expressions also identify forward-looking statements, but their absence does not mean that the statement is not forward-looking. The forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that may cause actual results to differ materially from those in the forward-looking statements. Factors that could affect actual results include risks associated with the initiation, timing, design, enrollment and cost of clinical trials; the fact that data from preclinical studies and Phase 1 or Phase 2 clinical trials may not necessarily be indicative of future clinical trial results; our ability to collect complete and audited data from clinical sites participating in our SMART trial; our ability to establish successful partnerships and collaborations with third parties; the regulatory approval process in the United States and other countries; and future capital requirements. For further information about these risks and other factors that may affect the actual results achieved by Pharmacyclics, please see the company's reports as filed with the U.S. Securities and Exchange Commission from time to time, including but not limited to its quarterly report on Form 10-Q for the quarter ended March 31, 2005. Forward-looking statements contained in this announcement are made as of this date, and we undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.