



# Pharmacyclics

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**PHARMACYCLICS ANNOUNCES DATA FROM PHASE 1 CLINICAL TRIAL  
OF ANTRIN<sup>®</sup> PHOTOTHERAPY FOR TREATMENT OF CORONARY  
ARTERY DISEASE**

***- Presentation at TCT Meeting Reports on Results of IVUS Imaging and  
Potential Use in Vulnerable Plaque -***

**Sunnyvale, Calif., -- October 4, 2004** -- Pharmacyclics, Inc. (Nasdaq: PCYC) today announced the presentation of Phase 1 trial results describing the use of Antrin<sup>®</sup> (motexafin lutetium) phototherapy for the treatment of coronary atherosclerosis. The presentation, by Dr. Alan Yeung, included data from intravascular ultrasound (IVUS) imaging studies showing that Antrin prevented plaque build-up following balloon angioplasty and stent placement in patients receiving optimum doses of drug and light therapy. Dr. Yeung's presentation took place at the Cardiovascular Research Foundation's 16th Annual Scientific Meeting of Transcatheter Cardiovascular Therapeutics (TCT) held in Washington, DC, at a scientific session entitled, "Vulnerable Plaque: Pathophysiology, Detection and Therapeutic Intervention."

Angiographic data from the Phase 1 study, published in the September 16, 2003 issue of *Circulation*, provided initial evidence of the safety and feasibility of Antrin phototherapy in patients undergoing balloon angioplasty with stent deployment. The current study, reported at TCT, presented quantitative and qualitative results from IVUS imaging studies and represents the first observations detailing the morphological changes of the

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coronary arterial wall subjected to phototherapy with various doses of Antrin and light.

"Antrin phototherapy is safe and feasible as an adjunctive therapy after coronary stenting in patients with coronary artery disease," stated Dr. Yeung, division head of Cardiovascular Medicine and Professor at Stanford University and one of the investigators on the trial. "One study cohort showed suppression of plaque volume increase using an optimal drug-light regimen. The potential of this dose combination for atraumatic stabilization of vulnerable plaque should be further evaluated in a randomized controlled study to determine clinical efficacy."

During the open label multi-center drug and light dose escalation study, Antrin was administered intravenously to 79 patients 18-24 hours prior to balloon angioplasty and stent insertion for coronary atherosclerosis. Intravascular photoactivation of Antrin was accomplished using an optical fiber inserted into the coronary artery at the time of balloon angioplasty. In a sub-study involving 39 patients, careful qualitative and quantitative IVUS imaging was performed immediately after the procedure and at six months follow-up. Analysis of the IVUS data was based on serial slices through the treated arterial segment and untreated boundaries.

The design of the trial was based on preclinical studies, which suggest that Antrin may localize to plaque, prevent cell proliferation following arterial injury, selectively deplete macrophages (inflammatory cells) from plaque, and cause regression in plaque volume without damaging the vascular wall.

The IVUS analysis provided additional data that suggests Antrin does not have deleterious effects on the vessel wall. In the group of patients (N=7) receiving 2-4 mg/kg of Antrin and 100 Joules of light, no atherosclerotic plaque volume increase was

observed at the stented site at six month follow-up (average plaque area  $8.01 \pm 4.33 \text{ mm}^2$  post stent to  $7.86 \pm 3.24 \text{ mm}^2$  at six months, not significant,  $P=0.79$ ). Statistically significant plaque volume increases were observed in the stented arterial segments in the two other patient cohorts receiving lower doses of Antrin (0-1.0 mg/kg, N=9, average plaque area  $6.59 \pm 2.28 \text{ mm}^2$  post stent to  $7.17 \pm 2.47 \text{ mm}^2$  at six months,  $P=0.028$ ) and higher doses of light (200-600 Joules, N=23, average plaque area  $7.76 \pm 3.70 \text{ mm}^2$  post stent to  $8.91 \pm 3.87 \text{ mm}^2$  at six months,  $P<0.001$ ).

Similar results have been reported in animal models which indicate that Antrin phototherapy with low doses of light produce more favorable effects.

"The detection and treatment of vulnerable plaque represents an emerging area in cardiology," said Richard A. Miller, M.D., president and chief executive officer of Pharmacyclics. "The IVUS data reported here demonstrate that Antrin phototherapy produces a favorable biologic effect in coronary arteries and we intend to pursue the application of our technology to diagnosis and treatment of vulnerable plaque."

#### **About Atherosclerosis and Vulnerable Plaque**

Atherosclerosis is a major cause of morbidity and death. The disease occurs through build-up of cholesterol and abnormal tissue within blood vessel walls, which often leads to life-threatening blockages of blood vessels to the heart and brain. Coronary atherosclerosis is often treated with balloon angioplasty and stents, which are techniques that mechanically enlarge and maintain the coronary lumen. Frequently, a build-up of plaque occurs at the site of stent implantation.

Although atherosclerosis has long been known to be associated with high levels of circulating cholesterol, inflammation has been shown to be another important factor in

progression of atherosclerosis and in plaque rupture, a cause of heart attacks. Inflammatory lesions in the walls of coronary arteries, known as vulnerable plaque, are prone to rupture causing acute thrombosis and obstruction of blood flow and heart attacks. Vulnerable plaque is not readily detected by current imaging techniques such as angiography since it usually does not limit blood flow. Intravascular ultrasound is a sensitive imaging technique that allows for detailed evaluation of the vessel wall and lumen size. Unlike angiography, which does not visualize the vessel wall, IVUS provides the ability to measure plaque size and vessel wall characteristics.

### **About Antrin**

Antrin is injected into the bloodstream, where it is designed to selectively accumulate in sites of plaque throughout the body. Targeted areas are then exposed to far-red light, which is delivered by an optical fiber inserted into the vessel using standard interventional techniques. When activated by the light, Antrin generates a chemical reaction that may selectively eliminate macrophages, causing stabilization or reduction of vulnerable plaque. Antrin phototherapy has completed Phase 1 and Phase 2 testing in peripheral arterial disease, and Phase 1 testing in coronary artery disease. These trials indicated that intravenous administration of Antrin and the Antrin phototherapy procedure are well tolerated, with no serious adverse events seen in the over 200 patients enrolled in these studies.

### **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.pcyc.com](http://www.pcyc.com). Pharmacyclics<sup>®</sup>, Antrin<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, 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 and 2 clinical trials may not necessarily be indicative of future clinical trial results; the company's 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 annual report on Form 10-K for the period ended June 30, 2004. 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.

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